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FILE 'SCISEARCH' ENTERED AT 16:54:05 ON 10 AUG 2005

FILE 'CAPLUS' ENTERED AT 16:54:05 ON 10 AUG 2005

=> s collagen conjugate
L1 44 COLLAGEN CONJUGATE

=> s l1 and TGF beta
L2 1 L1 AND TGF BETA

=> d l2 cbib abs

L2 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN
1994:253359 Document No. 120:253359 Biocompatible polymer conjugates of natural polymers. Rhee, Woonza; Wallace, Donald G.; Michaels, Alan S.; Burns, Ramon A., Jr.; Fries, Louis; Delustro, Frank; Bentz, Hanne; Mccullough, Kimberly; Damani, Ramesh; Berg, Richard A. (Collagen Corp., USA). PCT Int. Appl. WO 9401483 A1 19940120, 103 pp. DESIGNATED STATES: W: AU, JP; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1993-US6292 19930701. PRIORITY: US 1992-907518 19920702; US 1992-922541 19920730; US 1992-984933 19921202; US 1992-984197 19921202; US 1992-985680 19921202; US 1993-25032 19930302.

AB Non-immunogenic conjugates are formed by covalently binding a biol. inactive, natural polymer or derivative thereof to synthetic hydrophilic polymers, e.g. PEG, via specific types of chemical bonds. The biocompatible conjugates can be used for soft tissue augmentation and for coating or forming various articles. The compns. may include other components such as liquid, pharmaceutically acceptable carriers to form injectable formulations, and/or biol. active proteins such as growth factors or cytokines. A solution of transforming growth factor β1 (**TGF**-. **beta.**1) was added to a solution of difunctionally activated PEG and the mixture was allowed to react for 2 min at 17°. To this solution was added a fibrillar atelopeptide collagen solution and the resulting mixture allowed to incubate overnight at ambient temperature to form pellets comprising collagen-PEG-**TGF**-β 1 conjugate. After washing the pellets 6 times with phosphate buffer .apprx.50% of **TGF**-.

beta.1 was retained in the composition

=> s l1 and angiotensin II
L3 0 L1 AND ANGIOTENSIN II

=> s l1 and IGF
L4 0 L1 AND IGF

=> s l1 and insulin like growth factor
L5 3 L1 AND INSULIN LIKE GROWTH FACTOR

=> dup remove l5
PROCESSING COMPLETED FOR L5
L6 3 DUP REMOVE L5 (0 DUPLICATES REMOVED)

=> d l6 1-3 cbib abs

L6 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
1994:253359 Document No. 120:253359 Biocompatible polymer conjugates of natural polymers. Rhee, Woonza; Wallace, Donald G.; Michaels, Alan S.; Burns, Ramon A., Jr.; Fries, Louis; Delustro, Frank; Bentz, Hanne; Mccullough, Kimberly; Damani, Ramesh; Berg, Richard A. (Collagen Corp., USA). PCT Int. Appl. WO 9401483 A1 19940120, 103 pp. DESIGNATED STATES: W: AU, JP; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1993-US6292 19930701. PRIORITY: US 1992-907518 19920702; US 1992-922541 19920730; US 1992-984933 19921202; US 1992-984197 19921202; US 1992-985680 19921202; US 1993-25032 19930302.

AB Non-immunogenic conjugates are formed by covalently binding a biol. inactive, natural polymer or derivative thereof to synthetic hydrophilic polymers, e.g. PEG, via specific types of chemical bonds. The biocompatible conjugates can be used for soft tissue augmentation and for coating or forming various articles. The compns. may include other components such as liquid, pharmaceutically acceptable carriers to form injectable formulations, and/or biol. active proteins such as growth factors or cytokines. A solution of transforming growth factor β1 (TGF-β1) was added to a solution of difunctionally activated PEG and the mixture was allowed to react for 2 min at 17°. To this solution was added a fibrillar atelopeptide collagen solution and the resulting mixture allowed to incubate overnight at ambient temperature to form pellets comprising collagen-PEG-TGF-β1 conjugate. After washing the pellets 6 times with phosphate buffer .apprx.50% of TGF-β1 was retained in the composition

L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
1994:708312 Document No. 121:308312 Collagen-polymer conjugates for nonimmunogenic compositions and soft tissue augmentation. Rhee, Woonza; Wallace, Donald G.; Michaels, Alan S.; Burns, Ramon A., Jr.; Fries, Louis; Delustro, Frank; Bentz, Hanne (Collagen Corp., USA). U.S. US 5328955 A 19940712, 20 pp. Cont.-in-part of U.S. 5,162,430. (English). CODEN: USXXAM. APPLICATION: US 1992-922541 19920730. PRIORITY: US 1988-274071 19881121; US 1989-433441 19891114.

AB Pharmaceutically acceptable, nonimmunogenic compns. are formed by covalently binding atelopeptide collagens to pharmaceutically pure, synthetic, hydrophilic polymers via specific types of chemical bonds to provide collagen/polymer conjugates. The atelopeptide collagen can be type I, II, or III and may be fibrillar or nonfibrillar. The synthetic hydrophilic polymer may be polyethylene glycol and derivs. thereof having a weight average mol. weight 100-20,000. The compns. may include other components such as liquid, pharmaceutically acceptable carriers to form injectable formulations, and/or biol. active proteins such as growth factors. The collagen-polymer conjugates of the invention generally contain large amts. of water when formed. The conjugates can be dehydrated to form a relatively solid object. The dehydrated, solid object can be ground into

particles which can be suspended in a nonaq. fluid such as an oil and injected for the purpose of providing soft tissue augmentation. Once in place, the particles rehydrate and expand in size five fold or more. For example, difunctional PEG succinimidyl glutarate was prepared and treated with collagen solution to obtain a microgel of random size fibrils.

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
1994:307541 Document No. 120:307541 Collagen-polymer tubes for use in vascular surgery. Rhee, Woonza; McCullough, Kimberly (Collagen Corp., USA). U.S. US 5292802 A 19940308, 19 pp. Cont.-in-part of U.S. Ser. No. 922,541. (English). CODEN: USXXAM. APPLICATION: US 1992-985680 19921202. PRIORITY: US 1988-274071 19881121; US 1989-433441 19891114; US 1992-922541 19920730.
AB Medical articles in the form of tubes as artificial veins and artery are formed by covalently binding collagen to synthetic and hydrophilic polymers such as PEG via specific types of chemical bonds to provide collagen-polymer conjugates which are used to make the tubes. The tubes can be surgically implanted and attached to, or implanted within, a channel in a mammal for the purpose of repairing the channel. Collagen in phosphate buffer pH =7.4 was reacted with succinimidyl glutarate (preparation given) and the mixture left at 1-22° for 15 hs. The solution was then centrifuged and the resulting pellets of reconstituted fibrils collected and washed and used to make tubes for artificial vasculature. Collagen-PEG conjugates had reduced immunogenicity in guinea pigs as compared to bovine collagen. Conjugates of transforming growth factor β2 with collagen-PEG are prepared

=> s l1 and ascorbic acid
L7 0 L1 AND ASCORBIC ACID

=> s l1 and vitamin C
L8 0 L1 AND VITAMIN C

=> s hydrogel conjugate
L9 10 HYDROGEL CONJUGATE

=> dup remove l9
PROCESSING COMPLETED FOR L9
L10 7 DUP REMOVE L9 (3 DUPLICATES REMOVED)

=> d l10 1-7 cbib abs

L10 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
2005:490570 Bioresponsive Hydrogel Microlenses. Kim, Jongseong; Nayak, Satish; Lyon, L. Andrew (School of Chemistry and Biochemistry, Georgia Institute of Technology, Atlanta, GA, 30332-0400, USA). Journal of the American Chemical Society, 127(26), 9588-9592 (English) 2005. CODEN: JACSAT. ISSN: 0002-7863. Publisher: American Chemical Society.
AB The authors report investigations of bioresponsive hydrogel microlenses as a new protein detection technol. Stimuli-responsive poly(N-isopropylacrylamide-co-acrylic acid) (pNIPAm-co-AAc) microgels have been synthesized via free-radical precipitation polymerization These hydrogel microparticles were then functionalized with biotin via EDC coupling. Hydrogel microlenses were prepared from the particles via Coulombic assembly onto a silane-modified glass substrate. Arrays containing both pNIPAm-co-AAc microgels (as an internal control) and biotinylated pNIPAm-co-AAc microgels were then used to detect multivalent binding of both avidin and polyclonal anti-biotin. Protein binding was determined by monitoring the optical properties of the microlenses using a bright-field optical microscopy technique. The microlens method is shown to be very specific for the target protein, with no detectable interference from nonspecific protein binding. Finally, the reversibility of the hydrogel microlens assay has been studied in the case of anti-biotin to determine the potential

application of the microlens assay technol. in a displacement-type assay. These results suggest that the microlens method may be an appropriate one for label-free detection of proteins or small mols. via displacement of tethered protein-ligand pairs.

L10 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
2002:964899 Document No. 138:44758 Polysaccharide-based polymerizable hydrogels for medical applications. Massia, Stephen; Trudel, Julie; Burdick, Julie-anne M. (USA). U.S. Pat. Appl. Publ. US 2002192182 A1 20021219, 5 pp. (English). CODEN: USXXCO. APPLICATION: US 2002-95722 20020312. PRIORITY: US 2001-PV275546 20010312.

AB A hydrogel is provided in which varying ratios of acryloyl dextran mols. and acryloyl hyaluronan products are crosslinked to form a **hydrogel conjugate.** The incorporation of the derivatized hyaluronan mols. allows a hydrogel to be constructed which may be degraded by hydrolysis and enzymic pathways. This mechanism offers novel hydrogel which may be useful in medical applications including the prevention of surgical adhesions, controlled drug delivery, tissue coatings, tissue adherence, and tissue supporting structures, and the coating of medical devices and related articles prior to placement within a patient. Dextran and hyaluronan were sep. converted into an acryloyl derivative by treatment with glycidyl methacrylate in dimethylaminopyridine solution A gel was prepared by the mixing the above 2 acryloylated polysaccharides and photopolymn. The present hydrogel, having varying proportions of derivatized dextran and hyaluronan may be degraded by hydrolysis. This ability allows for a non-enzymic release mechanism in addition to conventional enzymic release and breakdown of the hyaluronan backbone polymer.

L10 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
2001:886568 Document No. 136:42803 Conjugate addition reactions for the controlled delivery of pharmaceutically active compounds. Hubbel, Jeffrey A.; Elbert, Donald; Schoenmakers, Ronald (Eidgenossische Technische Hochschule Zurich, Switz.; Universitat Zurich). PCT Int. Appl. WO 2001092584 A1 20011206, 221 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US18101 20010604. PRIORITY: US 2000-586937 20000602.

AB The invention features polymeric biomaterials formed by nucleophilic addition reactions to conjugated unsatd. groups. These biomaterials may be used for medical treatments.

L10 ANSWER 4 OF 7 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 1
2001:651855 The Genuine Article (R) Number: 461NR. One-step synthesis of a fluorescent phospholipid-**hydrogel conjugate** for driving self-assembly of supported lipid membranes. Ng C C; Cheng Y L (Reprint); Pennefather P S. Univ Toronto, Dept Chem Engn & Appl Chem, Toronto, ON M5S 3E5, Canada (Reprint); Univ Toronto, Dept Pharmaceut Sci, Toronto, ON M5S 3E5, Canada. MACROMOLECULES (14 AUG 2001) Vol. 34, No. 17, pp. 5759-5765. ISSN: 0024-9297. Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036 USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We have synthesized a phospholipid-**hydrogel conjugate** that appears to drive the self-assembly of lipid membranes. A one-step radical polymerization synthesis of the conjugate was devised using lipid anchors that contain a fluorescent marker and a reactive vinyl group. The anchors preferentially located at oil-water interfaces during hydrogel formation and through their vinyl groups became

covalently attached at the hydrogel surface. X-ray photoelectron spectroscopy and laser scanning confocal microscopy confirmed surface localization of the anchors. Upon mixing the conjugates with liposomes, lipid membranes readily self-assembled around the lipid-modified hydrogel surfaces. Control experiments with anchorless hydrogels indicate that anchors influenced the surface density and morphology of the lipid membranes. The one-step synthesis allows for simple control of surface anchor density and thus potential control of lipid membrane properties; the fluorescent markers facilitate anchor quantitation and further membrane interaction studies. Potential applications include high throughput drug screening, diagnostics, cell models, and drug delivery.

L10 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
2002:350625 Document No. 138:95486 Conjugate addition reactions for the controlled delivery of pharmaceutically active compounds. Schoenmakers, R.; Elbert, D.; Van De Wetering, P.; Hubbell, J. (Institute for Biomedical Engineering, ETH and University of Zurich, Zurich, CH-8044, Switz.). Proceedings - 28th International Symposium on Controlled Release of Bioactive Materials and 4th Consumer & Diversified Products Conference, San Diego, CA, United States, June 23-27, 2001, Volume 2, 1305-1306. Controlled Release Society: Minneapolis, Minn. (English) 2001. CODEN: 69CNY8.

AB A new versatile method has been developed to couple drugs via a hydrolyzable linker to a polymer support using a conjugate addition reaction. Using this method the release of a paclitaxel model compound from its PEG3400 conjugate was found to have a half life time of 80 h.

L10 ANSWER 6 OF 7 MEDLINE on STN DUPLICATE 2
2001635083. PubMed ID: 11336385. Synthetic hydrogels as carriers in antisense therapy: preliminary evaluation of an oligodeoxynucleotide covalent conjugate with a copolymer of 1-vinyl-2-pyrrolidinone and 2-hydroxyethyl methacrylate. Lou X; Garrett K L; Rakoczy P E; Chirila T V. (Lions Eye Institute, Department of Biomaterials & Polymer Research, University of Western Australia, Nedlands, Australia.) Journal of biomaterials applications, (2001 Apr) 15 (4) 307-20. Journal code: 8813912. ISSN: 0885-3282. Pub. country: United States. Language: English.

AB A major challenge of the antisense therapeutic strategies is the development of improved systems for the delivery of antisense oligodeoxynucleotides (AS ODNs) in order to enhance the cellular uptake, to assure a better efficiency in reaching the target tissue, and to provide sustained delivery over longer periods of time. Because the current methods for delivery (liposomes and cationic polymers) present some disadvantages, the attention was directed toward the use of neutral polymers as carriers for the AS ODNs. Based on our previous work on synthetic hydrogels for vitreous substitution, we developed a poly[1-vinyl-2-pyrrolidinone-co-(2-hydroxyethyl methacrylate)] hydrogel as a potential carrier for AS ODNs. We have previously demonstrated that such hydrogels are not cytotoxic, and they may have growth-promoting effects on cultured fibroblasts. This copolymer also has the advantage of being injectable. In this study, a specific AS ODN was synthesized and then covalently bound to the copolymer via carbodiimide coupling method. The resulting conjugate was subjected to in vitro release experiments over 46 days in the presence of bovine vitreous humor. Compared with the control (no enzyme present), a significant amount of covalently bound ODN was released from the ODN-**hydrogel conjugate**, suggesting the possibility of using such systems for the sustained delivery of AS ODNs.

L10 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
1999:317199 Document No. 130:357165 Delivery of polyethylene glycol-conjugated molecules from degradable hydrogels. Harris, J. Milton (Shearwater Polymers, Inc., USA). PCT Int. Appl. WO 9922770 A1 19990514, 29 pp. DESIGNATED STATES: W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,

LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US918 19980123. PRIORITY: US 1997-964972 19971105.

AB A degradable, chemical crosslinked PEG hydrogel is described for controlled release, by hydrolysis, of conjugates of substantially nonpeptidic polymers such as PEG with biol. active mols. For example, PEG and protein conjugates can be released in vivo from the hydrogels for therapeutic application. The crosslinked hydrogels are formed by reaction of (1) active branched derivs. of PEG with (2) amino groups on the biol. active mol. and with (3) amino groups on other PEG mols. or other nonpeptidic polymers containing hydrolyzable linkages such as carboxylate ester, phosphate ester, acetal, imine, ortho ester, peptide, anhydride, ketal, or oligonucleotide linkages in the PEG backbone. The hydrolytic breakdown rate can be controlled by variation of the hydrolyzable linkage and of the degree of bonding (branching) of the branched PEG. Thus, PhCH2(OCH2CH2)nOCH2CO2H was converted to the acid chloride with SOCl2 and condensed with PhCH2(OCH2CH2)nOH; the resulting PhCH2(OCH2CH2)nOCH2CO2(CH2CH2O)nCH2Ph was subjected to hydrogenolysis over Pd/C and condensed with disuccinimidyl carbonate to form NHS-O2C(OCH2CH2)nOCH2CO2(CH2CH2O)nCO2-NHS (NHS = N-hydroxysuccinimidyl).

```
=> s alginate conjugate
L11          43 ALGINATE CONJUGATE

=> s l11 and TGF
L12           0 L11 AND TGF

=> s l11 and matrix
L13           3 L11 AND MATRIX

=> dup remove l13
PROCESSING COMPLETED FOR L13
L14           3 DUP REMOVE L13 (0 DUPLICATES REMOVED)

=> d l14 1-3 cbib abs
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L14 ANSWER 1 OF 3 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

2004:253692 The Genuine Article (R) Number: 801QA. Synthesis and characterization of a biotin-**alginate conjugate** and its application in a biosensor construction. Polyak B; Geresh S; Marks R S (Reprint). Ben Gurion Univ Negev, Inst Appl Biosci, POB 653, IL-84105 Beer Sheva, Israel (Reprint); Ben Gurion Univ Negev, Inst Appl Biosci, IL-84105 Beer Sheva, Israel; Ben Gurion Univ Negev, Dept Biotechnol Engn, IL-84105 Beer Sheva, Israel. BIOMACROMOLECULES (MAR-APR 2004) Vol. 5, No. 2, pp. 389-396. ISSN: 1525-7797. Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036 USA. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Biotin was covalently coupled with alginate in an aqueous-phase reaction by means of carbodiimide-mediated activation chemistry to provide a biotin-**alginate conjugate** for subsequent use in biosensor applications. The synthetic procedure was optimized with respect to pH of the reaction medium (pH 6.0), the degree of uronic acid activation (20%), and the order of addition of the reagents. The biotin-**alginate conjugate** was characterized by titration with 2-anilinonaphthalene-6-sulfonic acid (2,6-ANS), 4-hydroxyazobene-2'-carboxylic acid (HABA) and by an HPSEC-MALLS analytical method as well as by FTIR and C-13 NMR spectroscopy. As a compromise between the need for a high percent of molar modification of the alginate, on one hand, and sufficient gelling capability, on the other hand, an optimal modification of 10-13% of biotin-alginate was used. The new biotin-**alginate**

conjugate was used for the encapsulation of bioluminescent reporter cells into microspheres. A biosensor was prepared by conjugating these biotinylated alginate microspheres to the surface of a streptavidin-coated optical fiber, and the performance of the biosensor was demonstrated in the determination of the antibiotic, mitomycin C as a model toxin.

L14 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
2002:409132 Document No. 136:391057 Drug release from polymer **matrixes** through mechanical stimulation. Lee, Kuen Yong; Mooney, David J. (The Regents of the University of Michigan, USA). U.S. Pat. Appl. Publ. US 2002064559 A1 20020530, 11 pp. (English). CODEN: USXXCO. APPLICATION: US 2001-983320 20011024. PRIORITY: US 2000-2000/PV243813 20001027.

AB A method for drug delivery and polymer **matrix** suited to the method are disclosed. The polymer **matrix** has reversibly bound thereto a drug or combination of drugs, and is capable of releasing the drug or combination of drugs in response to mech. stimulation of the polymer **matrix.** According to the method of this invention, such a polymer **matrix** is delivered to an in vivo locus, e.g., the site of a wound, trauma, etc., and mech. stimulation of said polymer **matrix** is effected in vivo, thereby releasing the drug or combination of drugs in the area of the in vivo locus. Alginate hydrogels were prepared comprising Protanal, Trypan blue as a model drug, and CaSO4. One group of the sample hydrogels were subjected to mech. stimulation comprising three cycles of compression/relaxation by using a mech. tester. Release of the trypan blue drug from the compressed hydrogels increased steadily over the course of compression/relaxation cycles.

L14 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
2002:127241 Document No. 137:237538 A preliminary investigation of modified alginates as a **matrix** for gene transfection in a HeLa cell model. Padmanabhan, Kiran; Smith, Timothy J. (Department of Physiology and Pharmacology, University of the Pacific School of Pharmacy and Health Sciences, Stockton, CA, 95211, USA). Pharmaceutical Development and Technology, 7(1), 97-101 (English) 2002. CODEN: PDTEFS. ISSN: 1083-7450. Publisher: Marcel Dekker, Inc..

AB Previous reports have demonstrated the effectiveness of chitosan as a transfection agent. These studies have noted the importance of polysaccharide backbone interactions with the cell surface as well as cationic groups in the transfection process. The present study focuses upon the potential utility of another polysaccharide hydrogel, alginic acid, as a transfection agent. Alginic acid was modified by carbodiimide-mediated linkage of several heterocyclic and aromatic amines to the carboxyl group of the alginate, giving the alginate polycationic characteristics through which binding to nucleic acids could be facilitated. The amines used for this modification include diaminoacridine, thionin, basic fuchsin, acridine yellow, and diaminomethyltriazine. Of all the conjugates tested, basic fuchsin-modified alginate produced the greatest increase in the transfection of a plasmid coding for β-galactosidase into HeLa cells. These studies demonstrate that other polysaccharide hydrogels can be used as transfection agents, and the structural orientation of the cationic spacer arm is crucial for effective transfection.

=> dup remove l11
PROCESSING COMPLETED FOR L11
L15 27 DUP REMOVE L11 (16 DUPLICATES REMOVED)

=> d l15 1-27 cbib abs

L15 ANSWER 1 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
2004:231028 Document No. 141:354981 Cell crosslinked hydrogels. Lee, Kuen Yong; Kong, Hyun Joon; Larson, Ronald G.; Mooney, David J. (Department of

Biologic & Materials Sciences, University of Michigan, Ann Arbor, MI, 48109, USA). PMSE Preprints, 90, 565 (English) 2004. CODEN: PPMRA9. ISSN: 1550-6703. Publisher: American Chemical Society.

AB The cell interactive peptide G4RGDSP was conjugated with Na alginate and gelation behavior studied. Results indicated that interactions between cell receptors and adhesion ligands can be exploited to form reversible gel systems. The cell d. and the number of ligands per polymer chain were critical variables in the formation of these gel structures. Reversible gelation features of these systems may be ideal for biomedical applications in which one desires to deliver cells into the body for regeneration of tissues of organs.

L15 ANSWER 2 OF 27 MEDLINE on STN DUPLICATE 1

2004113400. PubMed ID: 15002998. Synthesis and characterization of a biotin-**alginate conjugate** and its application in a biosensor construction. Polyak Boris; Geresh Shimona; Marks Robert S. (The Institute for Applied Biosciences and Department of Biotechnology Engineering, Ben-Gurion University of the Negev, PO Box 653, Beer Sheva 84105, Israel.) Biomacromolecules, (2004 Mar-Apr) 5 (2) 389-96. Journal code: 100892849. ISSN: 1525-7797. Pub. country: United States. Language: English.

AB Biotin was covalently coupled with alginate in an aqueous-phase reaction by means of carbodiimide-mediated activation chemistry to provide a biotin-**alginate conjugate** for subsequent use in biosensor applications. The synthetic procedure was optimized with respect to pH of the reaction medium (pH 6.0), the degree of uronic acid activation (20%), and the order of addition of the reagents. The biotin-**alginate conjugate** was characterized by titration with 2-anilinonaphthalene-6-sulfonic acid (2,6-ANS), 4-hydroxyazobene-2'-carboxylic acid (HABA) and by an HPSEC-MALLS analytical method as well as by FTIR and 13C NMR spectroscopy. As a compromise between the need for a high percent of molar modification of the alginate, on one hand, and sufficient gelling capability, on the other hand, an optimal modification of 10-13% of biotin-alginate was used. The new biotin-**alginate conjugate** was used for the encapsulation of bioluminescent reporter cells into microspheres. A biosensor was prepared by conjugating these biotinylated alginate microspheres to the surface of a streptavidin-coated optical fiber, and the performance of the biosensor was demonstrated in the determination of the antibiotic, mitomycin C as a model toxin.

L15 ANSWER 3 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN

2004:348874 Document No. 141:220902 Photodynamic actinometry using microspheres: concept, development and responsivity. Bisland, Stuart K.; Austin, James W.; Hubert, Daniel P.; Lilge, Lothar (Princess Margaret Hospital, Ontario Cancer Institute, Toronto, ON, M5G 2M9, Can.). Photochemistry and Photobiology, 79(4), 371-378 (English) 2004. CODEN: PHCBAP. ISSN: 0031-8655. Publisher: American Society for Photobiology.

AB Photodynamic therapy (PDT) relies on three main ingredients, oxygen, light and photoactivating compds., although the PDT response is definitively contingent on the site and level of reactive oxygen species (ROS) generation. This study describes the development of a novel, fluorescent-based actinometer microsphere system as a means of discerning spatially resolved dosimetry of total fluence and ROS production Providing a high resolution, localized, in situ measurement of fluence and ROS generation is critical for developing in vivo PDT protocols. Alginate-poly-L-lysine-alginate microspheres were produced using ionotropic gelation of sodium alginate droplets, ranging from 80 to 200 μm in diameter, incorporating two dyes, ADS680WS (ADS) and Rhodophyta-phycoerythrin (RPE), attached to the spheres' inside and outside layers, resp. To test the responsivity and dynamic range of RPE for ROS detection, the production of ROS was initiated either chemical using increasing concns. of potassium perchromate or photochem. using aluminum tetrasulfonated phthalocyanine. The generation of singlet oxygen was confirmed by phosphorescence at 1270 nm. The resulting photodegrdn. and decrease in fluorescence of RPE was found

to correlate with increased perchromate or PDT treatment fluence, resp. This effect was independent of pH (6.5-8) and could be inhibited using sodium azide. RPE was not susceptible to photobleaching with light alone (670 nm; 150 Jcm-2). ADS, which absorbs light between 600 and 750 nm, showed a direct correlation between radiant exposure (670 nm; 0-100 Jcm-2) and diminished fluorescence. Photobleaching was independent of irradiance (10-40 mW cm-2).

L15 ANSWER 4 OF 27 MEDLINE on STN DUPLICATE 2

2004496693. PubMed ID: 15376189. Peptide-modified alginate surfaces as a growth permissive substrate for neurite outgrowth. Dhoot Nikhil O; Tobias Chris A; Fischer Itzhak; Wheatley Margaret A. (School of Biomedical Engineering, Science and Health Systems, Drexel University, 32nd and Chestnut Streets, Philadelphia, PA 19104-2875, USA.) J Biomed Mater Res A, (2004 Nov 1) 71 (2) 191-200. Journal code: 101234237. ISSN: 1549-3296. Pub. country: United States. Language: English.

AB Different strategies are being investigated for treatment of spinal cord injuries, one of the most promising being application of neurotrophic factors, which have been shown to prevent neuronal death and stimulate regeneration of injured axons. Ex vivo gene therapy has emerged as the leading delivery method at the site of the injury, and we have shown previously that encapsulating genetically engineered fibroblasts in an immunoprotective alginate capsule can permit implantation of the factor-secreting cells without need for immunosuppression. This strategy could be greatly enhanced by providing the sprouting neurons with a permissive substrate upon which to attach and grow. We report here studies on the modification of an alginate gel surface by either coating it with laminin or by covalent attachment of YIGSR peptide. Using NB2a neuroblastoma cells, we found that native alginate elicited minimal cell attachment (approximately 1.5%); however, YIGSR-**alginate conjugate** elicited a fivefold increase in numbers of cells attached using peptide ratios of 0.5 and 1 mg/g alginate, ranging from 9.5% of the cells at the lower ratio, to about 44% at the higher. Only a further 19% increase was obtained at an increased peptide density of 2 mg/g alginate (approximately 63% over control). Laminin-coated gels showed approximately 60% cell attachment. However, laminin coating did not stimulate differentiation and neurite growth, whereas both numbers and lengths of outgrowths increased with increasing peptide density on peptide-modified alginate. We demonstrate here the ability of the peptide-modified alginate gels to allow adhesion of NB2a neuroblastoma cells and to promote neurite outgrowth from these cells when attached to the peptide-modified alginate surface. Also, we show that the adhesion of NB2a neuroblastoma cells and neurite outgrowth from the attached cells is a function of the peptide density on the gel surface.

L15 ANSWER 5 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN

2003:892641 Document No. 139:363590 Encapsulated cells to elicit immune response. Hortelano, Gonzalo (Canadian Blood Services, Can.). PCT Int. Appl. WO 2003092728 A1 20031113, 89 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-CA629 20030430. PRIORITY: US 2002-2002/PV377039 20020430.

AB The present invention provides a novel approach to vaccination and/or treatment using encapsulated cells for eliciting immune responses. More specifically, the present invention is to provide a method or process for inducing an immune response in a host, wherein the process comprises the steps of: enclosing genetically engineered antigen-producing cells comprising one or more transgene, into an immunoisolating implantable

device to provide encapsulated antigen-producing cells; introducing the encapsulated antigen-producing cells in the host; production of the transgene antigen product; bi-directional passage of the produced antigen product through the pores of the microcapsules, with preclusion of the passage of the antigen-producing cells therethrough; delivery of a continuous infusion of antigen to the host; activation of the immune system in response to the antigen.

L15 ANSWER 6 OF 27 MEDLINE on STN DUPLICATE 3

2003291833. PubMed ID: 12819072. Construction and characterization of a Pseudomonas aeruginosa mucoid exopolysaccharide-**alginate conjugate** vaccine. Theilacker Christian; Coleman Fadie T; Mueschenborn Simone; Llosa Nicolas; Grout Martha; Pier Gerald B. (Channing Laboratory, Department of Medicine, Harvard Medical School, Boston, Massachusetts 02115-5804, USA.) Infection and immunity, (2003 Jul) 71 (7) 3875-84. Journal code: 0246127. ISSN: 0019-9567. Pub. country: United States. Language: English.

AB Deterioration of lung function in patients with cystic fibrosis (CF) is closely associated with chronic pulmonary infection with mucoid Pseudomonas aeruginosa. The mucoid exopolysaccharide (MEP) from P. aeruginosa has been shown to induce opsonic antibodies in mice that are protective against this chronic infection. MEP-specific opsonic antibodies are also commonly found in the sera of older CF patients lacking detectable P. aeruginosa infection. When used in a human vaccine trial, however, MEP only minimally induced opsonic antibodies. To evaluate whether conjugation of MEP to a carrier protein could improve its immunogenicity, we bound thiolated MEP to keyhole limpet hemocyanin (KLH) by using succinimidyl-4-(N-maleimidomethyl)cyclohexane-1-carboxylate (SMCC) as a linker. In contrast to the native MEP polymer, the MEP-KLH conjugate vaccine induced high titers of MEP-specific immunoglobulin G (IgG) in C3H-HeN mice and in a rabbit. Sera from mice immunized with MEP-KLH conjugate, but not from animals immunized with comparable doses of native MEP, demonstrated opsonic killing activity. Vaccination with MEP-KLH conjugate induced opsonic antibodies broadly cross-reactive to heterologous mucoid strains of P. aeruginosa. Preexisting nonopsonic antibodies to MEP are found in normal human sera, including young CF patients, and their presence impedes the induction of opsonic antibodies. Induction of nonopsonic antibodies by either intraperitoneal injection of MEP or injection or feeding of the cross-reactive antigen, seaweed alginate, reduced the level of overall IgG elicited by follow-up immunization with the MEP-KLH conjugate. However, the opsonic activity was lower only in the sera of MEP-KLH conjugate-immunized mice with preexisting antibodies induced by MEP but not with antibodies induced by seaweed alginate. Immunization with MEP-KLH elicited a significant proportion of antibodies specific to epitopes involving O-acetate residues, and this subpopulation of antibodies mediated opsonic killing of mucoid P. aeruginosa in vitro. These results indicate that conjugation of MEP to KLH significantly enhances its immunogenicity and the elicitation of opsonic antibodies in mice and rabbits, that the conjugate induces opsonic antibodies in the presence of preexisting nonopsonic antibodies, and that opsonic antibodies to MEP are directed at epitopes that include acetate residues on the uronic acid polymer.

L15 ANSWER 7 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN

2002:409132 Document No. 136:391057 Drug release from polymer matrixes through mechanical stimulation. Lee, Kuen Yong; Mooney, David J. (The Regents of the University of Michigan, USA). U.S. Pat. Appl. Publ. US 2002064559 A1 20020530, 11 pp. (English). CODEN: USXXCO. APPLICATION: US 2001-983320 20011024. PRIORITY: US 2000-2000/PV243813 20001027.

AB A method for drug delivery and polymer matrix suited to the method are disclosed. The polymer matrix has reversibly bound thereto a drug or combination of drugs, and is capable of releasing the drug or combination of drugs in response to mech. stimulation of the polymer matrix. According to the method of this invention, such a polymer matrix is delivered to an in vivo locus, e.g., the site of a wound, trauma, etc.,

and mech. stimulation of said polymer matrix is effected in vivo, thereby releasing the drug or combination of drugs in the area of the in vivo locus. Alginate hydrogels were prepared comprising Protanal, Trypan blue as a model drug, and CaSO4. One group of the sample hydrogels were subjected to mech. stimulation comprising three cycles of compression/relaxation by using a mech. tester. Release of the trypan blue drug from the compressed hydrogels increased steadily over the course of compression/relaxation cycles.

L15 ANSWER 8 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
2002:688188 Document No. 137:237782 Temperature-responsive materials and their compositions for medical use. Tanihara, Masao; Yamaoka, Tetsuji; Mikami, Hiroshi; Kinoshita, Hisao (Sentomedo K. K., Japan; Japan Science and Technology Corporation). Jpn. Kokai Tokkyo Koho JP 2002256075 A2 20020911, 13 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 2001-54761 20010228.
AB The materials, useful for tissue adhesion prevention, tissue adhesives, wound dressings, hemostasis, and embolization, have skeletons of polysaccharides of non-animal origin and segments which agglomerate upon heating. N-isopropylacrylamide was polymerized onto starch in the presence of Ce(IV) diammonium nitrate to give a polymer, which formed a transparent solution at .apprx.25° and gelled at 37° in a phosphate buffer at pH 7.4.

L15 ANSWER 9 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
2002:734675 Document No. 138:390836 Engineering growing tissues. Alsberg, Eben; Anderson, Kenneth W.; Albeiruti, Amru; Rowley, Jon A.; Mooney, David J. (Department of Biomedical Engineering, University of Michigan, Ann Arbor, MI, 48109, USA). Proceedings of the National Academy of Sciences of the United States of America, 99(19), 12025-12030 (English) 2002. CODEN: PNASA6. ISSN: 0027-8424. Publisher: National Academy of Sciences.
AB Regenerating or engineering new tissues and organs may one day allow routine replacement of lost or failing tissues and organs. However, these engineered tissues must not only grow to fill a defect and integrate with the host tissue, but often they must also grow in concert with the changing needs of the body over time. We hypothesized that tissues capable of growing with time could be engineered by supplying growth stimulus signals to cells from the biomaterial used for cell transplantation. In this study, chondrocytes and osteoblasts were cotransplanted on hydrogels modified with an RGD-containing peptide sequence to promote cell multiplication. New bone tissue was formed that grew in mass and cellularity by endochondral ossification in a manner similar to normal long-bone growth. Transplanted cells organized into structures that morphol. and functionally resembled growth plates. These engineered tissues could find utility in treating diseases and injuries of the growth plate, testing the effect of exptl. drugs on growth-plate function and development, and investigating the biol. of long-bone growth. Furthermore, this concept of promoting the growth of engineered tissues could find great utility in engineering numerous tissue types by way of the transplantation of a small number of precursor cells.

L15 ANSWER 10 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
2002:209463 Document No. 137:252907 Alginate type and RGD density control myoblast phenotype. Rowley, Jon A.; Mooney, David J. (Department of Biomedical Engineering, Colleges of Engineering and Dentistry, University of Michigan, Ann Arbor, MI, USA). Journal of Biomedical Materials Research, 60(2), 217-223 (English) 2002. CODEN: JBMRBG. ISSN: 0021-9304. Publisher: John Wiley & Sons, Inc..
AB Alginates are being increasingly used for cell encapsulation and tissue engineering applications; however, these materials cannot specifically interact with mammalian cells. We have covalently modified alginates of varying monomeric ratio with RGD-containing cell adhesion ligands using carbodiimide chemical to initiate cell adhesion to these polymers. We hypothesized that we could control the function of cells adherent to RGD-modified alginate hydrogels by varying alginate polymer type and cell

adhesion ligand d., and we have addressed this possibility by studying the proliferation and differentiation of C2C12 skeletal myoblasts adherent to these materials. RGD d. on alginates of varying monomeric ratio could be controlled over several orders of magnitude, creating a range of surface densities from 1-100 fmol/cm2. Myoblast adhesion to these materials was specific to the RGD ligand, because adhesion could be competed away with soluble RGD in a dose-dependent manner. Myoblast proliferation and differentiation could be regulated by varying the alginate monomeric ratio and the d. of RGD ligands at the substrate surface, and specific combinations of alginate type and RGD d. were required to obtain efficient myoblast differentiation on these materials.

L15 ANSWER 11 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN

2002:127241 Document No. 137:237538 A preliminary investigation of modified alginates as a matrix for gene transfection in a HeLa cell model. Padmanabhan, Kiran; Smith, Timothy J. (Department of Physiology and Pharmacology, University of the Pacific School of Pharmacy and Health Sciences, Stockton, CA, 95211, USA). Pharmaceutical Development and Technology, 7(1), 97-101 (English) 2002. CODEN: PDTEFS. ISSN: 1083-7450. Publisher: Marcel Dekker, Inc..

AB Previous reports have demonstrated the effectiveness of chitosan as a transfection agent. These studies have noted the importance of polysaccharide backbone interactions with the cell surface as well as cationic groups in the transfection process. The present study focuses upon the potential utility of another polysaccharide hydrogel, alginic acid, as a transfection agent. Alginic acid was modified by carbodiimide-mediated linkage of several heterocyclic and aromatic amines to the carboxyl group of the alginate, giving the alginate polycationic characteristics through which binding to nucleic acids could be facilitated. The amines used for this modification include diaminoacridine, thionin, basic fuchsin, acridine yellow, and diaminomethyltriazine. Of all the conjugates tested, basic fuchsin-modified alginate produced the greatest increase in the transfection of a plasmid coding for β-galactosidase into HeLa cells. These studies demonstrate that other polysaccharide hydrogels can be used as transfection agents, and the structural orientation of the cationic spacer arm is crucial for effective transfection.

L15 ANSWER 12 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN

2001:935443 Document No. 136:58849 Compositions and methods to improve the oral absorption of antimicrobial agents. Choi, Seung-Ho; Lee, Jeoung-Soo; Keith, Dennis (Cubist Pharmaceuticals, Inc., USA; International Health Management Associates, Inc.; University of Utah Research Foundation). PCT Int. Appl. WO 2001097851 A2 20011227, 70 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US19625 20010618. PRIORITY: US 2000-598089 20000621; US 2001-829405 20010409; US 2001-PV283976 20010416.

AB The present invention provides compns. and methods for increasing absorption of antibacterial agents, particularly third generation cephalosporin antibacterial agents, in oral dosage solid and/or suspension forms. Specifically, the composition is comprised of a biopolymer that is preferably swellable and/or mucoadhesive, an antimicrobial agent, and a cationic binding agent contained within the biopolymer such that the binding agent is ionically bound or complexed to at least one member selected from the group consisting of the biopolymer and the antimicrobial agent. A solution of 44.5 mg calcium chloride in 10 mL water and 1.0 g of ceftriaxone in 10 mL water was added gradually to a solution of 400 mg carrageenan and the dispersion was centrifuged and the supernatant was

lyophilized. The resulting composition comprised carrageenan 27.7, ceftriaxone 1, and calcium chloride 3.1%. Plasma concentration of different antimicrobial-biopolymer complexes after oral administration to rats was measured.

L15 ANSWER 13 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
2001:617866 Document No. 135:185484 Modification of biopolymers for improved drug delivery. Calias, Pericles; Miller, Robert J. (Genzyme Corporation, USA). PCT Int. Appl. WO 2001060412 A2 20010823, 34 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US4925 20010215. PRIORITY: US 2000-PV182558 20000215; US 2000-PV211508 20000614.

AB A biol. active conjugate is disclosed comprising a biopolymer and a therapeutic agent joined by a disulfide bond. The conjugate, when formulated in a pharmaceutical composition with a suitable carrier, has improved in vivo stability and activity, and can be targeted to a variety of cells, tissues and organs. Thus, 3-nitro-2-pyridinesulfenylethylamine was allowed to react with hyaluronic acid in the presence of 1-hydroxybenzotriazole.

L15 ANSWER 14 OF 27 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
2002:223180 Document No.: PREV200200223180. Construction, characterization, and evaluation of immunogenicity and generation of opsonic antibody against mucoid Pseudomonas aeruginosa by an acetylated seaweed-**alginate conjugate** vaccine. Theilacker, C. [Reprint author]; Grout, M. [Reprint author]; Wang, Y. [Reprint author]; Pier, G. B. [Reprint author]. Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA. Abstracts of the General Meeting of the American Society for Microbiology, (2001) Vol. 101, pp. 335-336. print.
Meeting Info.: 101st General Meeting of the American Society for Microbiology. Orlando, FL, USA. May 20-24, 2001. American Society of Microbiology.
ISSN: 1060-2011. Language: English.

AB Mucoid P. aeruginosa produce a biofilm during infection in the cystic fibrosis (CF) lung which is mainly composed of mucoid exopolysaccharide (MEP) or alginate. MEP is a random polymer of D-mannuronic and L-guluronic acids linked beta 1-4 and differs from alginate produced by seaweed by virtue of its O-acteylation. To understand the mechanism of protection by opsonic antibodies directed against MEP we constructed a conjugate vaccine of acetylated seaweed-alginate. For this purpose we acetylated two different seaweed alginates with a high molecular weight and low guluronic acid content. NMR analysis confirmed an almost complete acetylation of free hydroxyl-groups (98%). The acetylated alginate was conjuguated with the EDC carbodiimide reagent to bovine serum albumin (BSA). Unbound BSA was removed by repeated ultrafiltration (500,000 Da MWCO) in deoxycholate-TRIS. The conjugates (BSA-ALG) contained 29% protein and 78% uronic acid and the molecular weight exceeded 2,000,000 Da. We immunized C3H-mice in groups of 5 with BSA-ALG and compared their responses to mice immunized with unconjugated acetylated alginate. There were no differences in post-immunization titers of IgM directed against acetylated alginate, while only mice immunized with BSA-ALG produced IgG antibodies directed against the polysaccharide. In addition, female New Zealand White rabbits were immunized with BSA-ALG. Sera derived from BSA-ALG-immunized rabbits had high IgG-titers against the alginate used for vaccination and against BSA. Both sera were also highly reactive to native MEP. ELISA plates coated with different whole mucoid P. aeruginosa bacteria showed high levels of IgG binding to all 6 strains tested. Opsonophagocytic killing activity of >50% was observed for the rabbit

sera-with titers ranging from 1:5-1:10 for the same mucoid strains. In summary, immunization with conjugates of acetylated seaweed alginate elicits IgG antibodies reactive to MEP that mediate opsonophagocytic killing of multiple mucoid P. aeruginosa strains.

L15 ANSWER 15 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
2001:657313 Document No. 135:370680 Modification of α-amylase by sodium alginate. Gomez, L.; Ramirez, H. L.; Villalonga, R. (Faculty of Agronomy Centre of Biotechnological Studies, University of Matanzas, Matanzas, C.P. 44740, Cuba). Acta Biotechnologica, 21(3), 265-273 (English) 2001. CODEN: ACBTDD. ISSN: 0138-4988. Publisher: Wiley-VCH Verlag Berlin GmbH.

AB Sodium alginate, activated by periodate oxidation, was covalently linked to porcine pancreatic α-amylase via reductive alkylation with NaBH4. The enzyme-polymer conjugate, purified by gel filtration on Fractogel EMD BioSEC (S), retained about 50% of the native specific amylolytic activity. The sugar content was estimated to be 712 mol of monosaccharides per mol of enzyme protein. An average of 11 amino groups out of 21 groups from α-amylase were modified with the polysaccharide. The functional stability was improved for α-amylase after conjugation with sodium alginate. In comparison with the native enzyme, the thermostability of α-amylase was increased by this modification. In addition, the stability in the range of pH 5.0-11.0 was improved for the modified enzyme. The conjugate was also more resistant to denaturation by 0.3% sodium dodecylsulfate, retaining about 10% of its initial activity after 120 min of incubation. The formation of stabilizing salt bridges in the protein surface of the α-amylase-polysaccharide complex was confirmed by FT-IR spectrometry. Attending to the results obtained, we conclude that the covalent attachment of the anionic polysaccharide sodium alginate to the enzymes might be a useful and non-expensive method for improving the stabilization of these biocatalysts under various denaturing conditions.

L15 ANSWER 16 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
1999:753117 Document No. 131:356082 Neutral or negatively charged polysaccharide compositions and methods for the delivery of nucleic acid molecules. Radhakrishnan, Ramachandran; Huang, Chin-Yi; Dwarki, Varavani J.; Murphy, John E. (Chiron Corporation, USA). PCT Int. Appl. WO 9959638 A2 19991125, 36 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US10697 19990514. PRIORITY: US 1998-PV85587 19980515.

AB Methods and compns. for the delivery of nucleic acids to cells in vivo are provided. The composition may comprise a recombinant or synthetic nucleic acid mol. in an aqueous solution comprising 0.5% to 5% (w/v) neutral or neg. charged polysaccharide, wherein said polysaccharide has an average mol. weight of between 1000 and 8000 daltons and may be maltodextrin.

L15 ANSWER 17 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
1998:217922 Document No. 128:269775 Emulsion properties of casein-alginate mixtures. Hwang, Jae-Kwan; Choi, Moon-Jung; Kim, Chong-Tai (Bioproducts Res. Center, Yonsei Univ., Seoul, 120-749, S. Korea). Han'guk Sikp'um Yongyang Kwahak Hoechi, 26(6), 1102-1108 (Korean) 1997. CODEN: HSYHFB. ISSN: 1226-3311. Publisher: Korean Society of Food Science and Nutrition.

AB Proteins and polysaccharides confer distinct functional properties in food systems. This research was attempted to improve emulsion properties of casein by protein-polysaccharide conjugation, in which alginates with various mol. weight were employed as polysaccharide sources. Casein-alginate mixts. were conjugated by the amino-carbonyl or Maillard reaction at

60°C and 79% relative humidity. The resulting casein-**alginate conjugates** were tested for their emulsion activity and emulsion stabilizing properties. In general, the emulsion stability of casein-alginate mixture greatly increased due to the amino-carbonyl reaction between casein and alginates, whose magnitude depended on the mol. weight of alginate, weight ratio of casein to alginate and incubation time. It was also found that thermal stability and pH stability were markedly improved by the casein-alginate conjugation.

L15 ANSWER 18 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
1995:682205 Document No. 123:93159 Synthesis, controlled-release properties and antitumor activity of alginate-cis-aconityl-daunomycin conjugates. Al-Shamkhani, Aymen; Duncan, Ruth (Cancer Res. Campaign's Polymer-Controlled Drug Delivery Res. Group, Univ. Keele, Keele, ST5 5BG, UK). International Journal of Pharmaceutics, 122(1,2), 107-19 (English) 1995. CODEN: IJPHDE. ISSN: 0378-5173. Publisher: Elsevier.
AB Covalent conjugates of alginate and the antitumor agent daunomycin (DNM) were synthesized to be stable in the circulation and allow release of the drug in the acidic milieu of the endosomal and lysosomal compartments of tumor cells or the slightly acidic extracellular fluid or some solid tumors. Alginates containing primary amine groups were first prepared by reacting alginate with excess ethylenediamine. DNM was first treated with cis-aconitic anhydride to produce N-cis-aconityl-DNM and then subsequently bound to the amino-modified alginate using the water-soluble carbodiimide 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide. High (Mw = 250,000) and low (Mw = 61 000) mol. weight alginate-DNM conjugates were prepared In vitro release studies showed that DMN was released from the conjugates (approx. 22-60%/48 h) under acidic conditions (pH 5 and 6) with minimal release occurring at neutral pH (approx. 2-4%/48 h). Reversed-phase HPLC confirmed that DNM was the only product released from high mol. weight alginate-DNM conjugate (22% released/48 h at pH 5), but the low mol. weight alginate-DNM released in addition a DNM derivative (approx. 60% released (total)/48 h at pH 5). In a preliminary experiment to investigate the antitumor activity of alginate-DNM conjugate in vivo, administration of a single i.p. injection of low mol. weight alginate-DNM (equivalent to 5 mg/kg DNM) to mice bearing B16 s.c. tumors resulted in a small, but significant delay in the growth of the tumor.

L15 ANSWER 19 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
1994:587305 Document No. 121:187305 Alginate-bioactive agent conjugates with acid-labile biodegradable spacer. Al-Shamkhani, Aymen; Duncan, Ruth (Keele University, UK). Brit. UK Pat. Appl. GB 2270920 A1 19940330, 31 pp. (English). CODEN: BAXXDU. APPLICATION: GB 1992-20294 19920925.
AB An alginate-bioactive agent is diclosed which has an acid labile biodegradable spacer linkage (e.g. a cis-aconityl group). The conjugate is effective for delivering bioactive agents (e.g. drugs) to targets existing in low-pH environments, either at the target surface or in the target interior. Antitumor activity of an alginate-cis-aconityl daunomycin conjugate was tested in melanoma-bearing mice. The increase in life span was greater in mice receiving the conjugate than in mice receiving either free daunomycin or a mixture of daunomycin and alginate. Some animals receiving free daunomycin showed signs of toxicity; none of the animals receiving the conjugate showed signs of toxicity.

L15 ANSWER 20 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
1993:567730 Document No. 119:167730 Alginic acid-thrombin conjugates, their preparation, and their uses as hemostatics and hemostatic goods. Nakano, Hitomi; Nakagiri, Nobuo; Fujita, Kotaro (Sakai Chemical Industry Co, Japan). Jpn. Kokai Tokkyo Koho JP 05163157 A2 19930629 Heisei, 6 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1991-334853 19911218.
AB Hemostatics and hemostatic medical goods (e.g. gauzes) contain alginic acid-thrombin conjugates prepared by treatment of alginic acid with active ester-forming agents in the presence of H2O-soluble carbodiimides, followed by treatment of the resulting active esters with thrombin. Na alginate

was treated with N-ethyl-N'-(3-dimethylaminopropyl)carbodiimide HCl salt and N-hydroxysuccinimide in H2O at room temperature for 40 min, then treated with aqueous thrombin solution at 4° for 18 h to give 99% alginic acid-thrombin conjugates, vs. 51%, when prepared similarly but without N-hydroxysuccinimide. The conjugate showed relative activity 0.53 unit/μg, vs. 0.44 unit/μg, for thrombin itself. The conjugates-containing powders were formulated.

L15 ANSWER 21 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
1994:100518 Document No. 120:100518 USe of immobilized β-glucosidase in the hydrolysis of cellulose. Woodward, J.; Koran, L. J., Jr.; Hernandez, L. J.; Stephan, L. M. (Chem. Technol. Div., Oak Ridge Natl. Lab., Oak Ridge, TN, 37831-6194, USA). ACS Symposium Series, 533(-Glucosidases), 240-50 (English) 1992. CODEN: ACSMC8. ISSN: 0097-6156.
AB The supplementation of com. produced Trichoderma reesei cellulases with β-glucosidases, which possess high specific activity toward cellobiose, should prove useful for increasing the rate and extent of the hydrolysis of cellulosic substrates. Since cellobiose is soluble, β-glucosidase could be used in an immobilized form and subsequently recovered and reused. Here, an immobilized β-glucosidase (Aspergillus niger) was prepared by entrapment within maintenance-free propylene glycol alginate/bone gelatin spheres. The enzyme thus immobilized was thermally stable at 40° for several months, during which time it could be used for the continuous hydrolysis of cellobiose without loss of efficiency. The data indicated there was no loss of β-glucosidase activity due to its leakage from the spheres. These biocatalytic spheres could also be dried (which makes them suitable for transporting) and subsequently rehydrated several times without any loss in catalytic activity. They were used to supplement a com. cellulase preparation for the hydrolysis of newsprint, recovered from the reaction mixture, and reused 9 times without appreciable loss in activity or conversion of cellulose to glucose.

L15 ANSWER 22 OF 27 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
1989:240657 Document No.: PREV198987121722; BA87:121722. A DOUBLE-BLIND STUDY OF HYPOSENSITIZATION WITH AN **ALGINATE CONJUGATE** EXTRACT OF DERMATOPHAGOIDES-PTERONYSSINUS CONJUVAC IN PATIENTS WITH PERENNIAL RHINITIS. CORRADO O J [Reprint author]; PASTORELLO E; OLLIER S; CRESSWELL L; ZANUSSI C; ORTOLANI C; INCORVAIA A; FUGAZZA A; LOVELY J R; ET AL. INQ: ROBERT J DAVIES, ACAD DEP RESPIRATORY MED, ST BARTHOLOMEW'S HOSP, LONDON, UK. Allergy (Copenhagen), (1989) Vol. 44, No. 2, pp. 108-115. CODEN: LLRGDY. ISSN: 0105-4538. Language: ENGLISH.
AB The efficacy of hyposensitization with a standardised extract of Dermatophagoides pteronyssinus (D. pteronyssinus) conjugated to alginate and containing known amounts of antigen P1 (Conjuvac) was tested in a double blind, placebo controlled, multi-centre study in 66 adult patients with perennial rhinitis. Patients received 11 weekly injections of increasing concentrations of Conjuvac containing from 56 + 101 to 448 + 103 IU D. pteronyssinus or placebo injections of the alginate diluent to some of which 5 μg of histamine has been randomly added. This was followed by 15 monthly injections of Conjuvac or placebo. The severity of nasal blockage, sneezing and rhinorrhoea was recorded twice daily in a diary and visual analogue assessments (VAS) made at each clinic visit. Nasal provocation testing (NPT) was performed with increasing concentrations of the same extract of D. pteronyssinus as used in the hyposensitization injections, and changes in nasal airways resistance measured by passive anterior rhinomanometry. VAS was recorded and NPT was performed on entry to the study and after the fifth, ninth and final monthly injection. Conjuvac injections were well tolerated. Large local reactions (> 5 cm) occurred within 30 min in only 1% of patients but later in 23%. No systemic reactions or anaphylaxis occurred within 30 min of injections, but urticaria or worsening of asthma and rhinitis was reported later in 3% of patients. A significant improvement in nasal obstruction

occurred in the Conjuvac compared to the placebo treated group ($P < 0.01$) and there was significant increase in the percentage of patients able to tolerate provocation with the highest concentrations of D. pteronyssinus extent after nine and 15 maintenance injections of Conjuvac compared to the placebo ($P < 0.02$, $P < 0.01$). Patient use of additional therapy decreased sooner in the Conjuvac treated group but was minimal in both groups after 5 months of the study.

L15 ANSWER 23 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
1985:556868 Document No. 103:156868 Soluble-insoluble polymers in enzyme immunoassay. Marshall, David L. (Seragen Diagnostics, Inc., USA). U.S. US 4530900 A 19850723, 5 pp. (English). CODEN: USXXAM. APPLICATION: US 1982-417281 19820913.
AB A method for determining the presence and amount of an antigen in solution is described in which (a) a soluble antibody-polymer conjugate reacts with the antigen and an antigen-enzyme conjugate forming a reaction product containing the polymer; (b) precipitating the polymer and separating the polymer from the test solution; (c) resolubilizing the product in a solution containing a substrate for the enzyme of the antigen-enzyme conjugate; and (d) measuring the enzyme activity and comparing it to enzyme activity in a solution having a known amount of antigen. Thus, an antibody-**alginate conjugate** was prepared by reacting activated alginate with the IgG fraction of rabbit antitheophylline serum at 4° overnight. The antitheophylline-**alginate conjugate** was diluted with Na alginate and allowed to react with theophylline-alkaline phosphatase conjugate. A dose response curve was generated by adding the antitheophylline-alkaline phosphatase conjugate to the theophylline serum stds. and theophylline-alkaline phosphatase conjugate. After 30 min at 37°, the alginate was made insol. with CaCl2. The tubes were centrifuged, the supernatant discarded, and 1 mL of p-nitrophenyl phosphate added to each pellet. The color which is produced is proportional to the amount of theophylline present in the samples.

L15 ANSWER 24 OF 27 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
1985:499742 The Genuine Article (R) Number: APV16. SKIN REACTIVITY OF **ALGINATE CONJUGATES** OF ARTEMISIA VULGARIS POLLEN EXTRACTS. WIHL J A. MALMO GEN HOSP, DEPT EAR NOSE & THROAT, S-21401 MALMO, SWEDEN. ANNALS OF ALLERGY (1985) Vol. 55, No. 2, pp. 381-381. ISSN: 0003-4738. Publisher: AMER COLL ALLERGY ASTHMA IMMUNOLOGY, 85 WEST ALGONQUIN RD SUITE 550, ARLINGTON HTS, IL 60005. Language: English.

L15 ANSWER 25 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
1983:85559 Document No. 98:85559 A new immunoassay separation technique using reversibly soluble polymers. Marshall, David L. (Dow Chem. Co., Indianapolis, IN, 46268, USA). Analytical Letters, 15(B18), 1457-65 (English) 1982. CODEN: ANALBP. ISSN: 0003-2719.
AB An immunoassay separation technique was developed based on the use of antibody-polymer conjugates with reversible solubility characteristics. Antibody was coupled to Na alginate with water-soluble carbodiimide. These conjugates could be used in place of unmodified antibody in various assay formats and removed from solution when desired by converting the polymer to an insol. form through pH adjustment or addition of metal ions. An enzyme immunoassay for theophylline was used to demonstrate the usefulness of the new approach for both manual and partially automated procedures.

L15 ANSWER 26 OF 27 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
1983:93837 Document No.: PREV198325018837; BR25:18837. ADJUVANT AND SUPPRESSIVE EFFECTS OF GRASS CONJUVAC AND OTHER **ALGINATE CONJUGATES** ON IMMUNO GLOBULIN G AND IMMUNO GLOBULIN E ANTIBODY RESPONSES IN MICE. TAYLOR W A [Reprint author]; SHELDON D; SPICER J W. RES DEP, MILES LAB LIMITED, STOKE POGES, SLOUGH, BERKSHIRE, ENGLAND, UK.

Allergy (Copenhagen), (1982) Vol. 37, No. SUPPL. 1, pp. 10-11.
Meeting Info.: PROCEEDINGS OF THE 14TH NORDIC CONGRESS OF ALLERGOLOGY, GOTHENBURG, SWEDEN, JUNE 10-13, 1981. ALLERGY.
CODEN: LLRGDY. ISSN: 0105-4538. Language: ENGLISH.

L15 ANSWER 27 OF 27 MEDLINE on STN DUPLICATE 4
82006188. PubMed ID: 7275187. Adjuvant and suppressive effects of Grass Conjuvac and other **alginate conjugates** on IgG and IgE antibody responses in mice. Taylor W A; Sheldon D; Spicer J W. Immunology, (1981 Sep) 44 (1) 41-50. Journal code: 0374672. ISSN: 0019-2805. Pub. country: ENGLAND: United Kingdom. Language: English.

AB BALB/c mice were immunized with grass pollen extract (GPE), GPE conjugated to sodium alginate (Conjuvac) or GPE absorbed to aluminium hydroxide gel (alum). Conjuvac was a more potent immunogen than the other two preparations of GPE when anti-GPE IgG antibody levels were compared. In contrast, the highest IgE antibody titres in the Conjuvac treated mice, were some sixteen-fold lower than the highest titres in the mice immunized with GPE in alum. The suppressive effects of Conjuvac on IgE antibody titres were also studied. Mice were immunized with 1 microgram dinitrophenyl (DNP)-GPE in alum and the anti-DNP and anti-GPE IgE antibody titres determined. After 4 and 5 weeks, the mice were injected with GPE or Conjuvac. The Conjuvac and the GPE failed to reduce the ongoing primary anti-GPE IgE responses but both suppressed the secondary responses by up to eight-fold. The suppression was not dose-related however. The ongoing primary and secondary anti-DNP IgE titres were suppressed in a dose-related manner by up to sixty-four fold by Conjuvac but GPE treatment was much less suppressive. We went on to investigate the suppressive properties of DNR-alginate (DNP-alg) conjugates. In these experiments mice were immunized with 1 microgram DNP-ovalbumin (DNP-OA) mixed with alum. After 4 and 5 weeks, the mice were injected with a dose of 6--600 micrograms DNP-alg with an average hapten density of 2 or 10 per alginate molecule. After a further 8 weeks a second injection of 1 microgram DNP-OA was given. All dose levels of both DNP-alg conjugates suppressed the continuing primary as well as the secondary anti-DNP IgE responses. It is concluded that alginate has properties similar to those of known T-cell adjuvants and that Conjuvac may prove useful in the immunotherapy of atopic allergy.

=> s hyaluronic acid conjugate
L16 80 HYALURONIC ACID CONJUGATE

=> s l16 and TGF
L17 1 L16 AND TGF

=> d l17 cbib abs

L17 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN
1994:253359 Document No. 120:253359 Biocompatible polymer conjugates of natural polymers. Rhee, Woonza; Wallace, Donald G.; Michaels, Alan S.; Burns, Ramon A., Jr.; Fries, Louis; Delustro, Frank; Bentz, Hanne; Mccullough, Kimberly; Damani, Ramesh; Berg, Richard A. (Collagen Corp., USA). PCT Int. Appl. WO 9401483 A1 19940120, 103 pp. DESIGNATED STATES: W: AU, JP; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1993-US6292 19930701. PRIORITY: US 1992-907518 19920702; US 1992-922541 19920730; US 1992-984933 19921202; US 1992-984197 19921202; US 1992-985680 19921202; US 1993-25032 19930302.

AB Non-immunogenic conjugates are formed by covalently binding a biol. inactive, natural polymer or derivative thereof to synthetic hydrophilic polymers, e.g. PEG, via specific types of chemical bonds. The biocompatible conjugates can be used for soft tissue augmentation and for coating or forming various articles. The compns. may include other components such as liquid, pharmaceutically acceptable carriers to form injectable formulations, and/or biol. active proteins such as growth factors or

cytokines. A solution of transforming growth factor β1 (**TGF**-β1) was added to a solution of difunctionally activated PEG and the mixture was allowed to react for 2 min at 17°. To this solution was added a fibrillar atelopeptide collagen solution and the resulting mixture allowed to incubate overnight at ambient temperature to form pellets comprising collagen-PEG-**TGF**-β1 conjugate. After washing the pellets 6 times with phosphate buffer .apprx.50% of **TGF**-β1 was retained in the composition

=> s polyethylene glycol conjugate
L18 900 POLYETHYLENE GLYCOL CONJUGATE

=> s l18 and TGF
L19 2 L18 AND TGF

=> dup remove l19
PROCESSING COMPLETED FOR L19
L20 2 DUP REMOVE L19 (0 DUPLICATES REMOVED)

=> d l20 1-2 cbib abs

L20 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
2002:429081 Document No. 137:16557 Protein and cDNA sequence of human transforming growth factor β-related proteins and their uses in diagnosis and therapy. Jing, Shuqian (Amgen, Inc., USA). PCT Int. Appl. WO 2002044379 A2 20020606, 126 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US44866 20011128. PRIORITY: US 2000-PV253476 20001128.

AB Full-length cDNAs encoding two human transforming growth factor β related protein (**TGF**-β-R) is provided. The invention also provides vectors, host cells, selective binding agents, and methods for producing **TGF**-β-R. Also provided for are methods for the treatment, diagnosis, amelioration, or prevention of diseases associated with **TGF**-β-R. The invention also relates to antibody for transforming growth factor β-related protein **TGF**-β-R and uses in diagnosis and therapy.

L20 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
2002:117502 Document No. 136:162339 High affinity RNA ligands for transforming growth factor β2 and their identification by SELEX. Pagratis, Nikos; Lochrie, Michael; Gold, Larry (Gilead Sciences, Inc., USA). U.S. US 6346611 B1 20020212, 89 pp., Cont.-in-part of U. S. 6,124,449. (English). CODEN: USXXAM. APPLICATION: US 1999-363939 19990729. PRIORITY: US 1991-714131 19910610; US 1992-931473 19920817; US 1992-964624 19921021; US 1993-117991 19930908; US 1995-434465 19950504; US 1995-458424 19950602; US 1998-46247 19980323.

AB Methods are described for the identification and preparation of high-affinity nucleic acid ligands to **TGF**.beta.2. Included in the invention are specific RNA ligands to **TGF**.beta.2 identified by the SELEX method. Also included are RNA ligands that inhibit the interaction of **TGF**.beta.2 with its receptor. The ligands have a number of diagnostic and therapeutic uses. The selection procedure is described in detail. Pharmacokinetics of a **polyethylene glycol conjugate** of one of the oligonucleotides are studied.

=> s l18 and insulin growth factor

L21 0 L18 AND INSULIN GROWTH FACTOR

=> s l18 and transplantation
L22 45 L18 AND TRANSPLANTATION

=> s l22 and cytokine
L23 5 L22 AND CYTOKINE

=> dup remove l23
PROCESSING COMPLETED FOR L23
L24 5 DUP REMOVE L23 (0 DUPLICATES REMOVED)

=> d l24 1-5 cbib abs

L24 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
2004:39584 Document No. 140:87695 A new member of the TNF ligand superfamily and its use in treating immune disorders. Ebner, Reinhard; Yu, Guo-Liang; Ruben, Steven M.; Zhai, Yifan; Ullrich, Stephen (Human Genome Sciences, Inc., USA). U.S. Pat. Appl. Publ. US 2004009147 A1 20040115, 189 pp., Cont.-in-part of U.S. 6,635,743. (English). CODEN: USXXCO. APPLICATION: US 2003-375680 20030228. PRIORITY: US 1996-PV13923 19960322; US 1996-PV30157 19961031; US 1997-822953 19970321; US 1998-3886 19980107; US 1998-27287 19980220; US 1998-PV75409 19980220; US 1999-252656 19990219; US 1999-PV124041 19990311; US 1999-PV137457 19990604; US 1999-PV142657 19990706; US 1999-PV148326 19990811; US 1999-PV168380 19991202; US 2000-2000/523323 20000310; US 2002-2002/PV360234 20020301.
AB A new member of the human TNF-Ligand superfamily, Apoptosis Inducing Mol. II (AIM II) is identified by sequence homol. for use in the treatment of immune disorders. The protein is a ligand for the TNF receptor TR6 and so may be used for the therapeutic induction of apoptosis or as a target for new drugs for the therapeutic inhibition of apoptosis. The invention further relates to screening methods for identifying agonists and antagonists of AIM II activity. Also provided are therapeutic methods for treating lymphadenopathy, aberrant bone development, autoimmune and other immune system diseases, graft vs. host disease, rheumatoid arthritis, osteoarthritis and to inhibit neoplasia, such as tumor cell growth.

L24 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
2002:353487 Document No. 136:364900 Construction, cloning, recombinant expression and therapeutic use of single-chain dimeric granulocyte colony-stimulating factor and other single-chain multimeric protein conjugates. Nissen, Torben Lauesgaard; Jensen, Anne Dam (Maxygen Aps, Den.; Maxygen Holdings Ltd.). PCT Int. Appl. WO 2002036626 A1 20020510, 108 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-DK724 20011101. PRIORITY: DK 2000-1647 20001102.
AB The invention relates to single-chain multimeric polypeptides comprising at least two units of a monomeric polypeptide linked via a peptide bond or a peptide linker, wherein the monomeric polypeptide is of a type that is biol. active in monomeric form, and to polypeptide conjugates having at least one non-polypeptide moiety covalently bound to an attachment group of the polypeptide. The polypeptide is preferably a granulocyte colony-stimulating factor (G-CSF) dimer bound to a polymer mol., preferably to one or more polyethylene glycol (PEG) mols. Construction and cloning of a synthetic gene encoding single-chain G-CSF dimer, expression of the single-chain G-CSF dimer in Saccharomyces cerevisiae and in CHO cells, purification of the recombinant single-chain G-CSF dimers from yeast and CHO cells, and covalent attachment of SPA-PEG to the purified single-chain G-CSF dimers are described. In vitro biol. activity of

non-conjugated and conjugated single-chain G-CSF dimers, and in vivo activity of the single-chain G-CSF dimers in healthy rats and in rats with chemotherapy-induced neutropenia are reported.

L24 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

2000:842003 Document No. 134:4058 Human tumor necrosis factor receptor 5 and its coding cDNA sequence. Wei, Ying-Fei; Ruben, Steven M.; Gentz, Reiner L.; Ni, Jian (Human Genome Sciences, Inc., USA). PCT Int. Appl. WO 2000071150 A1 20001130, 285 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US13515 20000518. PRIORITY: US 1999-PV135164 19990520.

AB The present invention relates to a novel human gene encoding a polypeptide which is a member of the tumor necrosis factor (TNF) receptor family, and has now been found to bind TRAIL. More specifically, an isolated cDNA mol. is provided encoding a human polypeptide named tumor necrosis factor receptor-5, sometimes referred to as "TNFR-5" or "TR5", and now referred to hereinafter as "TRAIL receptor without intracellular domain" or "TRID". The extracellular domain of TRID binds the cytotoxic ligand TRAIL (tumor necrosis factor-related apoptosis-inducing ligand) and blocks TRAIL-induced apoptosis. TRID polypeptides are also provided, as are vectors, host cells, and recombinant methods for producing the same. The invention further relates to screening methods for identifying agonists or antagonists of TRAIL polypeptide activity. Also provided are diagnostic and therapeutic methods utilizing such compns.

L24 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

1997:547405 Document No. 127:160574 The **cytokine** receptor WSX, agonist and antagonist ligands and their uses. Bennett, Brian; Carter, Paul J.; Chiang, Nancy Y.; Kim, Kyung Jin; Matthews, William; Rodrigues, Maria L. (Genentech, Inc., USA). PCT Int. Appl. WO 9725425 A1 19970717, 219 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US325 19970107. PRIORITY: US 1996-585005 19960108; US 1996-667197 19960620.

AB The **cytokine** receptor WSX that plays a role in hematopoiesis is identified and antibodies to it (including agonist and neutralizing antibodies) are disclosed and uses for them are described. Uses for WSX ligands (e.g., anti-WSX receptor agonist antibodies or OB protein) in hematopoiesis are also disclosed. The gene for the receptor was cloned using probes derived from a human liver expressed sequence tag to screen a Hep3B cDNA library and a full-length clone constructed from several overlapping clones. The receptor may play a role in control of cellular proliferation and it is expressed in fetus (lung, liver, kidney) and in adult (liver, placenta, lung, skeletal muscle, kidney, ovary, prostate, small intestine). A number of variants of the receptor were found, of which one (13.2) was a receptor for OB protein (leptin). OB protein was found to interact synergistically with interleukin 3, stem cell factor, and GM-CSF in hematopoiesis with a preferential stimulation of myelopoiesis. The identification of agonist antibodies is described.

L24 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

1995:911198 Document No. 124:263 Reduction of FK-506 requirements by combination with polyethylene glycol superoxide dismutase in orthotopic rat liver **transplantation.** Rao, Prakash N.; Cai, Xin;

Venkataramanan, Raman; Platt, Jeffrey L.; Demetris, Anthony; Thunberg, Allen; Faltynek, Connie; Starzl, Thomas; Kumar, Prem (Departments Surgery, University Pittsburgh, Pittsburgh, PA, USA). Journal of Allergy and Clinical Immunology, 95(6), 1276-81 (English) 1995. CODEN: JACIBY. ISSN: 0091-6749. Publisher: Mosby-Year Book.

AB Reperfusion after ischemia results in endothelial cell injury and Kupffer cell activation. Inflammatory **cytokines** thus released can induce major histocompatibility complex antigens and increase the immunogenicity of the graft. An orthotopic rat liver allotransplant model was used to test the hypothesis that prevention of reperfusion injury by infusion of polyethylene glycol superoxide dismutase (PEG-SOD) would result in long-term allograft survival in the presence of subthreshold immunosuppressive dosages. ACI rats were used as donors, and Lewis strain rats as recipients. Orthotopic liver **transplantation** was initially performed to identify a subthreshold dose of the immunosuppressant FK-506, which would be unable to extend survival longer than control untreated rats with this strain combination. After testing three i.m. FK-506 doses of 0.04, 0.08, and 0.16 mg/kg, it was observed that an FK-506 dose of 0.04 mg/kg/day for 14 days was unable to extend survival longer than in untreated recipients. This dose of FK-506 was used in combination with PEG-SOD at doses of 1000, 3000, 10,000, or 30,000 units. Recipient animals were treated i.v. with PEG-SOD as a loading dose to facilitate tissue penetration on day 1, and beginning on the day of **transplantation**, every 2 days for the duration of the study. Results of histol. studies and mean survival time were compared in untreated recipients and in rats treated with PEG-SOD plus 0.04 mg/kg/day FK-506. Mean survival time was increased significantly in these animals to 40.6 days as compared with either untreated rats (10.0 days) or rats treated with 0.04 mg/kg FK-506 alone (13.7 days). Histol. examination demonstrated a significant reduction in the cellular infiltrate in rats treated with PEG-SOD plus FK-506, as compared with recipients treated with either agent alone or left untreated. The results therefore suggest a potential approach to reducing immunosuppression in **transplantation.**

```
=> s cell encapsulation
L25       1219 CELL ENCAPSULATION

=> s l25 and collagen
L26         78 L25 AND COLLAGEN

=> s l26 and PEG
L27          8 L26 AND PEG

=> s l27 and TGF
L28          0 L27 AND TGF

=> dup remove l27
PROCESSING COMPLETED FOR L27
L29          7 DUP REMOVE L27 (1 DUPLICATE REMOVED)

=> d l29 1-7 cbib abs
```

L29 ANSWER 1 OF 7 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 1

2005170940 EMBASE Bioresponsive phosphoester hydrogels for bone tissue engineering. Wang D.-A.; Williams C.G.; Yang F.; Cher N.; Lee H.; Elisseeff J.H.. Dr. J.H. Elisseeff, Department of Biomedical Engineering, Johns Hopkins University, Clark Hall 106, 3400 North Charles Street, Baltimore, MD 21218, United States. jhe@bme.jhu.edu. Tissue Engineering Vol. 11, No. 1-2, pp. 201-213 2005.
Refs: 31.
ISSN: 1076-3279. CODEN: TIENFP
Pub. Country: United States. Language: English. Summary Language: English.

ED Entered STN: 20050512
AB Bioresponsive and intelligent biomaterials are a vehicle for manipulating cell function to promote tissue development and/or tissue engineering. A photopolymerized hydrogel based on a phosphoester-poly(ethylene glycol) polymer (PhosPEG) was synthesized for application to marrow-derived mesenchymal stem cell (MSC) encapsulation and tissue engineering of bone. The phosphor-containing hydrogels were hydrolytically degradable and the rate of degradation increased in the presence of a bone-derived enzyme, alkaline phosphatase. Gene expression and protein analysis of encapsulated MSCs demonstrated that PhosPEG-**PEG** cogels containing an intermediate concentration of phosphorus promoted the gene expression of bone-specific markers including type I **collagen**, alkaline phosphatase, and osteonectin, without the addition of growth factors or other biological agents, compared with pure poly(ethylene glycol)-based gels. Secretion of alkaline phosphatase, osteocalcin, and osteonectin protein was also increased in the PhosPEG cogels. Mineralization of gels increased in the presence of phosphorus in both cellular and acellular constructs compared with **PEG** gels. In summary, phosphate-**PEG**-derived hydrogels increase gene expression of bone-specific markers, secretion of bone-related matrix, and mineralization and may have a potential impact on bone-engineering therapies.

L29 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
2004:824796 Document No. 141:320084 Polymer gels for encapsulation of biological materials. Hubbell, Jeffrey A.; Pathak, Chandrashekhar P.; Sawhney, Amarpreet S.; Desai, Neil P.; Hossainy, Syed F. A. (USA). U.S. Pat. Appl. Publ. US 2004195710 A1 20041007, 34 pp., Cont.-in-part of U.S. Ser. No. 811,901, abandoned. (English). CODEN: USXXCO. APPLICATION: US 2004-761180 20040120. PRIORITY: US 1990-598880 19901015; US 1992-843485 19920228; US 1992-870540 19920420; US 1992-958870 19921007; US 1995-484160 19950607; US 1997-783387 19970113; US 2001-2001/811901 20010319.
AB This invention provides novel methods for the formation of biocompatible membranes around biol. materials using photopolymn. of water soluble mols. The membranes can be used as a covering to encapsulate biol. materials or biomedical devices, as a "glue" to cause more than one biol. substance to adhere together, or as carriers for biol. active species. Several methods for forming these membranes are provided. Each of these methods utilizes a polymerization system containing water-soluble macromers, species, which are at once polymers and macromols. capable of further polymerization The macromers are polymerized using a photoinitiator (such as a dye), optionally a cocatalyst, optionally an accelerator, and radiation in the form of visible or long wavelength UV light. The reaction occurs either by suspension polymerization or by interfacial polymerization The polymer membrane can be formed directly on the surface of the biol. material, or it can be formed on material, which is already encapsulated. For example, the microcapsule interfacial polymerization method was used to form membrane around alginate-poly(L-lysine) (PLL) microcapsules containing islets. Alginate-PLL coacervated microspheres, containing one or two human pancreatic islets each, were suspended in a 1.1% CaCl2 solution and aspirated free of excess solution to obtain a dense plug of microspheres. A solution of ethyl eosin (0.04% weight/volume) was prepared in a 1.1% CaCl2 solution and filter-sterilized. The plug of microspheres was suspended in 10 mL of the eosin solution for 2 min to allow uptake of the dye and excess dye. was removed. A solution of **PEG** 18.5 tetraacrylate (2 mL; 23% weight/volume) containing 100 L of a 3.5% weight/volume solution of triethanolamine in HEPES buffered saline was added to 0.5 mL of those microspheres. The microspheres were exposed to argon ion laser light for 30 s with periodic agitation, washed with calcium solution and the process was repeated in order to further stabilize the coating. A static glucose stimulation test (SGS) confirmed the vitality and functionality of the islets.

L29 ANSWER 3 OF 7 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
2004:325741 Document No.: PREV200400327407. Encapsulating Chondrocytes in degrading **PEG** hydrogels with high modulus: Engineering gel structural changes to facilitate cartilaginous tissue production. Bryant, Stephanie J.; Bender, Ryan J.; Durand, Kevin L.; Anseth, Kristi S. [Reprint Author]. Dept Chem Engn, Univ Colorado, Boulder, CO, 80309, USA. anseth@colorado.edu. Biotechnology and Bioengineering, (June 30 2004) Vol. 86, No. 7, pp. 747-755. print.
CODEN: BIBIAU. ISSN: 0006-3592. Language: English.

AB A major challenge when designing cell scaffolds for chondrocyte delivery in vivo is creating scaffolds with sufficient mechanical properties to restore initial function while simultaneously controlling temporal changes in the gel structure to facilitate tissue formation. To address this design challenge, degradable photocrosslinked hydrogels based on poly(ethylene glycol) were investigated. To alter the gel's initial mechanical properties, hydrogels were fabricated by varying the initial macromer concentration from 10% to 15% to 20%. A twofold increase in macromer concentration resulted in an eightfold increase in the initial compressive modulus from 60 to 500 kPa. Gel degradation was tailored by incorporating fast-degrading crosslinks that enable maximal extracellular matrix (ECM) diffusion with time and a minimal number of nondegrading (or slowly degrading) crosslinks to maintain scaffold integrity and prevent complete gel erosion during tissue formation. Chondrocytes encapsulated in these gels produced cartilaginous tissue rich in glycosaminoglycans and **collagen** as seen biochemically and histologically. Interestingly, mass loss appeared to more closely match tissue secretion in gels fabricated from a 15% macromer concentration. However, the spatial ECM distribution was grossly similar in all three gels. By tailoring gel degradation and controlling network evolution during degradation, gels with optimal properties can be fabricated to support initially physiologic compressive loads while simultaneously supporting the formation of a neotissue. Copyright 2004 Wiley Periodicals, Inc.

L29 ANSWER 4 OF 7 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
2003178589 EMBASE Tailoring the degradation of hydrogels formed from multivinyl poly(ethlene glycol) and poly(vinyl alcohol) macromers for cartilage tissue engineering. Martens P.J.; Bryant S.J.; Anseth K.S.. K.S. Anseth, Department of Chemical Engineering, University of Colorado, Boulder, CO 80309, United States. Kristi.Anseth@Colorado.edu. Biomacromolecules Vol. 4, No. 2, pp. 283-292 2003.
Refs: 46.
ISSN: 1525-7797. CODEN: BOMAF6
Pub. Country: United States. Language: English. Summary Language: English.

ED Entered STN: 20030519

AB Tuning the degradation profiles of polymer cell carriers to match cell and tissue growth is an important design parameter for (cartilage) tissue engineering. In this study, degradable hydrogels were fabricated from divinyl, tetrafunctional poly(ethylene glycol) (**PEG**) and multivinyl, multifunctional poly(vinyl alcohol) (PVA) macromers to form homopolymer and copolymer gels. These gels were characterized by their volumetric swelling ratio and mass loss profiles as a function of degradation time. By variation of the macromer chemistry and functionality, the degradation time, changed from less than 1 day for homopolymer PVA gels to 34 days for pure **PEG** gels. Furthermore, the degrading medium influenced mass loss, and a marked decrease in degradation time, from 34 to 12 days, was observed with the **PEG** gels when a chondrocyte-specific medium containing fetal bovine serum was employed. Interestingly, when copolymer gels of **PEG** and PVA were formed, PVA was released throughout the degradation (as determined by gel permeation chromatography) suggesting that covalent cross-linking of the PVA in the network was facilitated by copolymerizing with the **PEG** macromer. To assess these novel gels for cartilage tissue engineering applications, chondrocytes were photoencapsulated in the

copolymer networks and cultured in vitro for up to 6 weeks. DNA, glycosaminoglycan (GAG), and total **collagen** contents increased with culture time, and the resulting neocartilaginous tissue at 6 weeks was homogeneously distributed as seen histologically. Biochemical analysis revealed that the constructs were comprised of 0.66 ± 0.04 μg of DNA/mg wet weight (ww), 1.0 ± 0.05% GAG/ww, and 0.29 ± 0.07% total **collagen**/ww at 6 weeks. Furthermore, the compressive modulus increased during culture from 7 to 97 kPa as the neocartilaginous tissue evolved and the gel degraded. In summary, fabricating hydrogels through the copolymerization of **PEG** and PVA macromers is an effective tool for encapsulating chondrocytes, controlling gel degradation profiles, and generating cartilaginous tissue.

L29 ANSWER 5 OF 7 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

2003507252 EMBASE Controlling the spatial distribution of ECM components in degradable **PEG** hydrogels for tissue engineering cartilage.
Bryant S.J.; Anseth K.S.. K.S. Anseth, Department of Chemical Engineering, University of Colorado, ECCH 111, Boulder, CO 80309-0424, United States. kristi.anseth@colorado.edu. Journal of Biomedical Materials Research - Part A Vol. 64, No. 1, pp. 70-79 1 Jan 2003.
Refs: 29.
ISSN: 0021-9304. CODEN: JBMRCH
Pub. Country: United States. Language: English. Summary Language: English.

ED Entered STN: 20040116

AB In developing a scaffold to support new tissue growth, the degradation rate and mass loss profiles of the scaffold are important design parameters. In this study, hydrogels were prepared by copolymerizing a degradable macromer, poly(lactic acid)-b-poly(ethylene glycol)-b-poly(lactic acid) endcapped with acrylate groups (**PEG**-LA-DA) with a nondegradable macromer, poly(ethylene glycol) dimethacrylate (PEGDM). The resulting hydrogels exhibited a range of degradation behavior and mass loss profiles. Chondrocytes were photoencapsulated in gels formulated with 50:50, 25:75, and 15:85 (mol % PEGDM: mol % **PEG**-LA-DA) and cultured for 6 weeks in vitro. The neocartilaginous tissue formed was examined biochemically and histologically. After 6 weeks, the DNA content in gels with 75 and 85% degradable crosslinks was nearly twice that of the DNA content in the 50% gels. The total **collagen** content was significantly higher in the 85% gel [2.4 ± 0.8% wet weight (ww)] compared to the 50% gel (0.22 ± 0.29% ww). In examining the neocartilaginous tissue with immunohistochemistry, type II **collagen** was localized in the pericellular region in the 50% gel; however, when increased degradation was incorporated into the gel, type II **collagen** was found throughout the neotissue. In summary, the important role of hydrogel degradation in controlling and influencing the deposition and distribution of extracellular matrix molecules was demonstrated and quantified. .COPYRGT. 2002 Wiley Periodicals, Inc.

L29 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

1996:467217 Document No. 125:137244 Gels for encapsulation of biological materials. Hubbell, Jeffrey A.; Pathak, Chandrashekhar P.; Sawhney, Amarpreet S.; Desai, Neil P.; Hossainy, Syed F. A. (University of Texas System, USA). U.S. US 5529914 A 19960625, 34 pp., Cont.-in-part of U.S. Ser. No. 870, 540. (English). CODEN: USXXAM. APPLICATION: US 1992-958870 19921007. PRIORITY: US 1990-598880 19901015; US 1991-740632 19910805; US 1991-740703 19910805; US 1992-843485 19920228; US 1992-870540 19920420.

AB This invention provides novel methods for the formation of biocompatible membranes around biol. materials using photopolymn. of water-soluble mols. The membranes can be used as a covering to encapsulate biol. materials or biomedical devices, as a ''glue'' to cause >1 biol. substance to adhere together, or as carriers for biol. active species. Several methods for forming these membranes are provided. Each of these methods utilizes a polymerization system containing water-soluble macromers, species which are at once

polymers and macromols. capable of further polymerization The macromers are polymerized by using a photoinitiator (such as a dye), optionally a cocatalyst, optionally an accelerator, and radiation in the form of visible or long-wavelength UV light. The reaction occurs either by suspension polymerization or by interfacial polymerization The polymer membrane can be formed directly on the surface of the biol. material, or it can be formed on material which is already encapsulated.

L29 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
1989:150498 Document No. 110:150498 Process for encapsulation of living cells with protein. Tice, Thomas R.; Meyers, William E. (Stolle Research and Development Corp., USA). U.S. US 4798786 A 19890117, 7 pp. (English). CODEN: USXXAM. APPLICATION: US 1982-375710 19820506.
AB A process for encapsulation of living cells comprises (1) dispersing the cells in an aqueous solution of capsule wall-forming protein (e.g. albumins): (2) forming aqueous droplets of the dispersion in an aqueous-immiscible, cell-compatible continuous processing medium (e.g. vegetable oil): (3) crosslinking the protein with an agent which is soluble in the continuous processing medium but insol. in the aqueous droplets; and (4) enlarging pores in the capsule with a capsule-wall degrading enzyme. Hybridoma cells 106 were suspended in 0.5 mL RPMI 1640 culture media containing both serum albumin 100, **PEG** 200 mg, etc. This suspension was added dropwise to 20 mL sesame oil with stirring to form a water-in-oil emulsion. Sebacoyl chloride 0.2 mL in sesame oil was added to crosslink the albumin. After crosslinking the crosslinker was removed by washing with sesame oil. None of the encapsulated cells were stained with trypan blue. All stained with neutral red. The cells were viable for ≥2 mo.

=> s (west j?/au or mann b?/au)
L30 10636 (WEST J?/AU OR MANN B?/AU)

=> s l30 and ECM
L31 48 L30 AND ECM

=> s l31 and collagen
L32 16 L31 AND COLLAGEN

=> dup remove l32
PROCESSING COMPLETED FOR L32
L33 8 DUP REMOVE L32 (8 DUPLICATES REMOVED)

=> d l33 1-8 cbib abs

L33 ANSWER 1 OF 8 MEDLINE on STN DUPLICATE 1
2003381682. PubMed ID: 12918034. Enhancing mechanical properties of tissue-engineered constructs via lysyl oxidase crosslinking activity. Elbjeirami Wafa M; Yonter Edward O; Starcher Barry C; **West Jennifer L.** (Department of Biochemistry & Cell Biology, Rice University, 6100 Main Street, Houston, Texas 77005, USA.) J Biomed Mater Res A, (2003 Sep 1) 66 (3) 513-21. Journal code: 101234237. ISSN: 1549-3296. Pub. country: United States. Language: English.
AB A number of strategies have been investigated to enhance the mechanical stability of engineered tissues. In this study, we utilized lysyl oxidase (LO) to enzymatically crosslink extracellular matrix (**ECM**) proteins, particularly **collagen** and elastin, to enhance the mechanical integrity of the **ECM** and thereby impart mechanical strength to the engineered tissue. Vascular smooth muscle cells (VSMCs) were liposomally transfected with the LO gene. Both Northern and Western analyses confirmed increased LO expression. Increased LO activity was demonstrated using a fluorescent enzyme substrate assay and by observation of the presence of increased levels of desmosine, a product of LO crosslinking, in the **ECM**. The mechanical effects of altered

crosslink densities within tissue-engineered constructs were demonstrated in a VSMC-populated **collagen** gel model. When smooth muscle cells transfected with lysyl oxidase were seeded in **collagen** gels, the tensile strength and elastic modulus in these constructs increased by approximately two-fold compared to constructs seeded with mock-transfected VSMCs. Also, desmosine levels in the LO-populated **collagen** gels were higher than they were in mock-seeded gels, as demonstrated via immunohistochemical staining. Compositional analysis of the **ECM** deposited by the transformed cells showed similar **collagen** and elastin levels, and cell proliferation rates were similar as well, thus attributing increased mechanical properties to **ECM** crosslinking.

L33 ANSWER 2 OF 8 EMBASE
on STN
2003444908 EMBASE Tissue engineered small-diameter vascular grafts. Schmedlen R.H.; Elbjeirami W.M.; Gobin A.S.; **West J.L.**. Dr. J.L. West, Department of Bioengineering, Rice University, MS 142, 6100 Main Street, Houston, TX 77005-1892, United States. jwest@ruf.rice.edu. Clinics in Plastic Surgery Vol. 30, No. 4, pp. 507-517 2003.
Refs: 69.
ISSN: 0094-1298. CODEN: CPSUDA
Pub. Country: United States. Language: English. Summary Language: English.
ED Entered STN: 20031201
AB Arterial occlusive disease remains the leading cause of death in western countries and often requires vascular reconstructive surgery. The limited supply of suitable small-diameter vascular grafts has led to the development of tissue engineered blood vessel substitutes. Many different approaches have been examined, including natural scaffolds containing one or more **ECM** proteins and degradable polymeric scaffolds. For optimal graft development, many efforts have modified the culture environment to enhance **ECM** synthesis and organization using bioreactors under physiologic conditions and biochemical supplements. In the past couple of decades, a great deal of progress on TEVGs has been made. Many challenges remain and are being addressed, particularly with regard to the prevention of thrombosis and the improvement of graft mechanical properties. To develop a patent TEVG that grossly resembles native tissue, required culture times in most studies exceed 8 weeks. Even with further advances in the field, TEVGs will likely not be used in emergency situations because of the time necessary to allow for cell expansion, **ECM** production and organization, and attainment of desired mechanical strength. Furthermore, TEVGs will probably require the use of autologous tissue to prevent an immunogenic response, unless advances in immune acceptance render allogenic and xenogenic tissue use feasible. TEVGs have not yet been subjected to clinical trials, which will determine the efficacy of such grafts in the long term. Finally, off-the-shelf availability and cost will become the biggest hurdles in the development of a feasible TEVG product. Although many obstacles exist in the effort to develop a small-diameter TEVG, the potential benefits of such an achievement are exciting. In the near future, a nonthrombogenic TEVG with sufficient mechanical strength may be developed for clinical trials. Such a graft will have the minimum characteristics of biological tissue necessary to remain patent over a period comparable to current vein graft therapies. As science and technology advance, TEVGs may evolve into complex blood vessel substitutes. TEVGs may become living grafts, capable of growing, remodeling, and responding to mechanical and biochemical stimuli in the surrounding environment. These blood vessel substitutes will closely resemble native vessels in almost every way, including structure, composition, mechanical properties, and function. They will possess vasoactive properties and be able to dilate and constrict in response to stimuli. Close mimicry of native blood vessels may aid in the engineering of other tissues dependent upon vasculature to sustain function. With further understanding of the factors involved in

cardiovascular development and function combined with the foundation of knowledge already in place, the development of TEVGs should one day lead to improved quality of life for those with vascular disease and other life-threatening conditions.

L33 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
2002:157948 Document No. 136:205503 Tissue engineering scaffolds promoting matrix protein production. **West, Jennifer L.**; **Mann, Brenda K.** (Rice University, USA). PCT Int. Appl. WO 2002016557 A2 20020228, 25 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US26170 20010821. PRIORITY: US 2000-PV226771 20000821.
AB Matrix-enhancing mols., such as TGF-β, are conjugated to or immobilized on scaffolds to increase **ECM** production by cells for tissue engineering, tissue regeneration and wound healing applications. The matrix-enhancing mol. is conjugated to a tether, such as polyethylene glycol (PEG) monoacrylate, for attachment to a tissue engineering or cell growth scaffold. The matrix-enhancing mol. retains activity after attachment to the scaffold, and causes cells growing in or on the scaffold to increase extracellular matrix (**ECM**) production, without substantially increasing proliferation of the cells, even when the scaffold addnl. contains cell adhesion ligands. The increased **ECM** produced by the cells aids in maintaining the integrity of the scaffold, particularly when the scaffold is degradable, either by hydrolysis or by enzymic degradation For example, TNFβ was conjugated to polyethylene glycol by reacting TNFβ with acryloyl-PEG-N-hydroxysuccinimide in TRIS buffer (pH 8.5) for 2 h. The mixture was then lyophilized and stored frozen. Smooth muscle cells were cultured in presence of 0.04 pmol/mL acryloyl-PEG-TGFβ and production of extracellular matrix protein was evaluated.

L33 ANSWER 4 OF 8 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
2002:371013 Document No.: PREV200200371013. Tissue engineered vascular grafts: Effects of bioactive scaffolds and mechanical stimulation. **West, Jennifer L.** [Reprint author]. Bioengineering, Rice University, 6100 S. Main Street, Houston, TX, 77584, USA. FASEB Journal, (March 22, 2002) Vol. 16, No. 5, pp. A1251. print.
Meeting Info.: Annual Meeting of Professional Research Scientists on Experimental Biology. New Orleans, Louisiana, USA. April 20-24, 2002.
CODEN: FAJOEC. ISSN: 0892-6638. Language: English.
AB Tissue engineered vascular grafts have been developed using bioactive hydrogel scaffolds and culturing the constructs in pulsatile flow bioreactors. The scaffold materials are degraded by proteolytic enzymes involved in tissue remodeling, promote cell adhesion via grafted adhesion peptides, and present tethered growth factors to optimize tissue formation. Upon culture in a shear and cyclic strain environment, smooth muscle cells within the construct become aligned circumferentially and increase their expression of **collagen** and elastin. Additionally, crosslinking of **ECM** proteins is increased, resulting in formation of stronger tissues.

L33 ANSWER 5 OF 8 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
2002:315488 The Genuine Article (R) Number: 537JV. Cell migration through defined, synthetic extracellular matrix analogues. Gobin A S; **West J L (Reprint)**. Rice Univ, Dept Bioengn, 6100 Main St, MS 142, Houston, TX 77005 USA (Reprint); Rice Univ, Dept Bioengn, Houston, TX 77005 USA. FASEB JOURNAL (MAR 2002) Vol. 16, No. 3, pp. U1-U16. ISSN: 0892-6638. Publisher: FEDERATION AMER SOC EXP BIOL, 9650 ROCKVILLE PIKE, BETHESDA, MD

20814-3998 USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We have developed synthetic hydrogel extracellular matrix (**ECM**) analogues that can be used to study mechanisms involved in cell migration, such as receptor-ligand interactions and proteolysis. The biomimetic hydrogels consist of bioinert polyethylene glycol diacrylate derivatives with proteolytically degradable peptide sequences included in the backbone of the polymer and adhesive peptide sequences grafted to the network. Hydrogels have been developed that degrade as cells secrete proteolytic enzymes. Adhesive peptide sequences grafted to the hydrogel provide ligands that can interact with receptors on the cell surface to mediate adhesion and spreading. In this study, we have characterized the effects of adhesive ligand density on fibroblast migration through collagenase-degradable and plasmin-degradable hydrogels and on smooth muscle cell migration through elastase-degradable hydrogels. In all three cases, we found that cell migration has a biphasic dependence on adhesion ligand concentration, with optimal migration at intermediate ligand levels. Furthermore, both adhesive and proteolytically degradable sequences were required for cell migration to occur. These synthetic **ECM** analogues may be useful for 3-D mechanistic studies of many aspects of cell migration.

L33 ANSWER 6 OF 8 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

2001:759700 The Genuine Article (R) Number: 474FD. Smooth muscle cell growth in photopolymerized hydrogels with cell adhesive and proteolytically degradable domains: synthetic **ECM** analogs for tissue engineering . **Mann B K**; Gobin A S; Tsai A T; Schmedlen R H; **West J L (Reprint)**. Rice Univ, Dept Bioengn, 6100 Main St, MS 142, Houston, TX 77005 USA (Reprint); Rice Univ, Dept Bioengn, Houston, TX 77005 USA. BIOMATERIALS (NOV 2001) Vol. 22, No. 22, pp. 3045-3051. ISSN: 0142-9612. Publisher: ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Photopolymerizable polyethylene glycol (PEG) derivatives have been investigated as hydrogel tissue engineering scaffolds. These materials have been modified with bioactive peptides in order to create materials that mimic some of the properties of the natural extracellular matrix (**ECM**). The PEG derivatives with proteolytically degradable peptides in their backbone have been used to form hydrogels that are degraded by enzymes involved in cell migration, such as collagenase and elastase. Cell adhesive peptides, such as the peptide RGD, have been grafted into photo polymerized hydrogels to achieve biospecific cell adhesion. Cells seeded homogeneously in the hydrogels during photopolymerization remain viable, proliferate. and produce **ECM** proteins. Cells can also migrate through hydrogels that contain both proteolytically degradable and cell adhesive peptides. The biological activities of these materials can be tailored to meet the requirements of a given tissue engineering application by creating a mixture of various bioactive PEG derivatives prior to photopolymerization. (C) 2001 Elsevier Science Ltd. All rights reserved.

L33 ANSWER 7 OF 8 MEDLINE on STN DUPLICATE 2

1999065673. PubMed ID: 9847287. Alveolar hypoxia increases gene expression of extracellular matrix proteins and platelet-derived growth factor-B in lung parenchyma. Berg J T; Breen E C; Fu Z; Mathieu-Costello O; **West J B.** (Department of Medicine, University of California San Diego, La Jolla, California, USA.) American journal of respiratory and critical care medicine, (1998 Dec) 158 (6) 1920-8. Journal code: 9421642. ISSN: 1073-449X. Pub. country: United States. Language: English.

AB The walls of pulmonary capillaries are extremely thin, and wall stress increases greatly when capillary pressure rises. Alveolar hypoxia causes pulmonary vasoconstriction and hypertension, and if this is uneven, some capillaries may be exposed to high transmural pressure and develop stress failure. There is evidence that increased wall stress causes capillary

remodeling. In this study we exposed Madison strain Sprague-Dawley rats to normobaric hypoxia (10% oxygen) for 6 h or 3 d (short-term group), and for 3 d or 10 d (long-term group). Peripheral lung tissue was then collected and messenger RNA (mRNA) levels were determined for extracellular matrix (**ECM**) proteins and growth factors. **Collagen** content (hydroxyproline) was also measured. Levels of mRNA for alpha2(IV) procollagen increased sixfold after 6 h of hypoxia and sevenfold after 3 d of hypoxia, and then decreased after 10 d exposure. Levels of mRNA for platelet-derived growth factor-B (PDGF-B) doubled after 6 h of hypoxia but returned to control values after 3 d. mRNA levels for alpha1(I) and alpha1(III) procollagens and fibronectin were increased after 3 d of hypoxia (by seven- to 12-fold, 1.6- to eightfold, and 12-fold, respectively), then decreased toward control values after 10 d. In contrast, neither levels of mRNA for vascular endothelial growth factor (VEGF) nor **collagen** content changed. These results suggest that alveolar hypoxia causes vascular remodeling in lung parenchyma, and are consistent with capillary wall remodeling in response to increased wall stress.

L33 ANSWER 8 OF 8 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 3
1997:522332 The Genuine Article (R) Number: XJ677. High lung inflation increases mRNA levels of **ECM** components and growth factors in lung parenchyma. Berg J T (Reprint); Fu Z X; Breen E C; Tran H C; MathieuCostello O; **West J B.** UNIV CALIF SAN DIEGO, DEPT MED 0623A, LA JOLLA, CA 92093. JOURNAL OF APPLIED PHYSIOLOGY (JUL 1997) Vol. 83, No. 1, pp. 120-128. ISSN: 8750-7587. Publisher: AMER PHYSIOLOGICAL SOC , 9650 ROCKVILLE PIKE, BETHESDA, MD 20814. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Remodeling of pulmonary capillaries occurs after chronic increases in capillary pressure (e.g., mitral stenosis). Also, remodeling of pulmonary arteries begins within 4 h of increased wall stress and is endothelium dependent. We have previously shown that high lung inflation increases wall stress in pulmonary capillaries. This study was designed to determine whether high lung inflation induces remodeling of the extracellular matrix (**ECM**) in lung parenchyma. Open-chest rabbits were ventilated for 4 h with 9-cmH(2)O positive end-expiratory pressure (PEEP) on one lung and 1-cmH(2)O PEEP on the other (High-PEEP group), or with 2-cmH(2)O PEEP on both lungs (Low-PEEP group). An additional untreated control group was also included. We found increased levels of mRNA in both lungs of High-PEEP rabbits (compared with both the Low-PEEP and untreated groups) for alpha(1)(III) and alpha(2)(IV) procollagen, fibronectin, basic fibroblast growth factor, and transforming growth factor-beta(1). In contrast, alpha(2)(I) procollagen and vascular endothelial growth factor mRNA levels were not changed. We conclude that high lung inflation for 4 h increases mRNA levels of **ECM** components and growth factors in lung parenchyma.

```
=> s tissue engineering
L34      23182 TISSUE ENGINEERING

=> s l34 and collagen conjugate
L35          2 L34 AND COLLAGEN CONJUGATE

=> dup remove l35
PROCESSING COMPLETED FOR L35
L36          2 DUP REMOVE L35 (0 DUPLICATES REMOVED)

=> d l36 1-2 cbib abs
```

L36 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
2002:205103 Document No. 136:252531 Glycosaminoglycan-polycation conjugates as matrix for tissue regeneration and their manufacture. Tanaka, Junzo; Taguchi, Satoshi; Miyazaki, Kyosuke; Sakura, Yoshiyuki; Otsuka, Tatsuo;

Bandai, Yoshinobu (Foundation for Scientific Technology Promotion, Japan; National Institute for Research In Inorganic Materials; Seikagaku Kogyo Co., Ltd.; Nitta Gelatin, Inc.). Jpn. Kokai Tokkyo Koho JP 2002080501 A2 20020319, 9 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 2000-273187 20000908.

AB The conjugates, which are molded into desired shapes and used as matrixes for helping regeneration of cartilage, liver, blood vessel, nerve, etc., are manufactured by crosslinking glycosaminoglycans such as hyaluronic acid and polycations such as type II collagen using water-soluble carbodiimide (WSC) as a condensing agent under a condition where no polyion complexes are not formed. Aqueous solution of WSC was added dropwise to a mixture of hyaluronic acid, type II collagen, HCl, and NaCl and the reaction mixture was let stand at 30° for 2 h. The gel thus obtained was washed with H2O for 2 days to remove the condensing agent, byproducts, Na, and Cl and freeze-dried for 1 day to give a matrix. The matrix was useful for culture of calf chondrocytes.

L36 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN

2000:102376 Document No. 132:241895 Modification of the adhesive properties of collagen by covalent grafting with RGD peptides. Myles, Jennifer L.; Burgess, Brian T.; Dickinson, Richard B. (Department of Chemical Engineering & Biomedical Engineering Program, University of Florida, Gainesville, FL, 32611, USA). Journal of Biomaterials Science, Polymer Edition, 11(1), 69-86 (English) 2000. CODEN: JBSEEA. ISSN: 0920-5063. Publisher: VSP BV.

AB Collagen, either alone or in combination with other materials, is an important natural biomaterial that is used in a variety of **tissue -engineering** applications. Cell adhesion and migration of cells within collagen-based biomaterials may be controlled by modifying the adhesive properties of collagen. Furthermore, spatially controlling the adhesiveness of the collagen may allow controlled localization or redistribution of cells. A method is presented for covalently coupling peptides that contain the well-characterized arginine-glycine-aspartic acid adhesion sequence directly to type I collagen monomers prior to fibrillogenesis. A heterobifunctional coupling agent was used to create stable amide and disulfide bonds with the lysine residues of the collagen monomers and the cysteine termini of the peptide mols., resp. The degree of conjugation could be controlled by changing the reaction conditions (ratios of reactants added and the length of incubation). The microstructure and gelation times of gels composed of covalently modified collagen were similar to those of unmodified gels. Cell adhesion on adsorbed monolayers of modified collagen was quantified using a well-established clonal cell line (K1735 murine melanoma). Cell adhesion was found to increase with both increasing degree of conjugation and increasing ratio of modified to unmodified collagen.

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=> s tissue scaffold
L37        403 TISSUE SCAFFOLD

=> s l37 and collagen conjugate
L38          0 L37 AND COLLAGEN CONJUGATE

=> s l37 and collagen
L39         97 L37 AND COLLAGEN

=> s l39 and PEG
L40          0 L39 AND PEG

=> s l39 and TGF
L41          6 L39 AND TGF

=> dup remove l41
PROCESSING COMPLETED FOR L41
L42           2 DUP REMOVE L41 (4 DUPLICATES REMOVED)
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=> d l42 1-2 cbib abs

L42 ANSWER 1 OF 2 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 1
1998:82894 Document No.: PREV199800082894. **Collagen** and heparin matrices for growth factor delivery. Schroeder-Tefft, J. A. [Reprint author]; Bentz, H.; Estridge, T. D.. Res. Dev., Collagen Corp., 2500 Faber Place, Palo Alto, CA 94303, USA. Journal of Controlled Release, (Dec. 15, 1997) Vol. 49, No. 2-3, pp. 291-298. print.
CODEN: JCREEC. ISSN: 0168-3659. Language: English.
AB Transforming growth factor-beta 2 (**TGF**-beta2) loses biological activity under physiological conditions as measured by its loss of activity in phosphate buffered saline (PBS), pH 7.4 at 37degree C. Studies were carried out to determine if **TGF**-beta2 could be stabilized by the production of a heparin/**TGF**-beta2 (Hep/**TGF**-beta2) complex. In vitro studies showed that Hep/**TGF**-beta2 remained active and **TGF**-beta2 alone lost activity, when stored for 2 months in PBS at 37degree C, as measured by a Mink lung bioassay. These findings show the utility of using a heparin/**TGF**-beta2 complex to stabilize the **TGF**-beta2. Stable Hep/**TGF**-beta2 complex was mixed with injectable fibrillar **collagen** for use as a **tissue scaffold** material. **Collagen** and **TGF**-beta2 formulations were tested for in vivo activity in a rat subcutaneous model. Forty-five animals were implanted with two injections of fibrillar **collagen** (FC), fibrillar **collagen** with heparin and guinea pig serum albumin (FC/Hep/GSA), fibrillar **collagen** with **TGF**-beta2 (FC + **TGF**-beta2), or fibrillar **collagen** with heparin/**TGF**-beta2 complex (FC + Hep/**TGF**-beta). Five animals were explanted at day 7, 21 and 42. The FC + Hep/**TGF**-beta2 formulation and FC + **TGF**-beta2, admixed formulation both produced increased extracellular matrix deposition and activation of cells in vivo. The ability of the FC + Hep/**TGF**-beta2 complex to recruit fibroblasts and produce new connective tissue locally, demonstrates the **TGF**-beta2 activity of the FC + Hep/**TGF**-beta2 complex in vivo.

L42 ANSWER 2 OF 2 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 2
97216963 EMBASE Document No.: 1997216963. **Collagen** and heparin matrices for growth factor delivery. Schroeder-Tefft J.A.; Bentz H.; Estridge T.D.. J.A. Schroeder-Tefft, Research and Development, Collagen Corporation, 2500 Faber Place, Palo Alto, CA 94303, United States. jacci-schroeder@collagen.com. Journal of Controlled Release Vol. 48, No. 1, pp. 29-33 1997.
Refs: 19.
ISSN: 0168-3659. CODEN: JCREEC
S 0168-3659(97)00055-2. Pub. Country: Netherlands. Language: English.
Summary Language: English.
ED Entered STN: 970807
AB Transforming growth factor-beta 2 (**TGF**-β2) loses biological activity under physiological conditions as measured by its loss of activity in phosphate buffered saline (PBS), pH 7.4 at 37°C. Studies were carried out to determine if **TGF**-β2 could be stabilized by the production of a heparin/**TGF**- β2 (Hep/**TGF**-β2) complex. In vitro studies showed that Hep/**TGF**-β2 remained active and **TGF**-β2 alone lost activity, when stored for 2 months in PBS at 37°C, as measured by a Mink lung bioassay. These findings show the utility of using a heparin/**TGF**-β2 complex to stabilize the **TGF**-β2. Stable Hep/**TGF**- β2 complex was mixed with injectable fibrillar **collagen** for use as a **tissue scaffold** material. **Collagen** and **TGF**-β2 formulations were tested for in vivo activity in a rat subcutaneous model.

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---Logging off of STN---

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Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	303.81	304.02

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-32.12	-32.12

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